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ORIGINAL CONTRIBUTIONS

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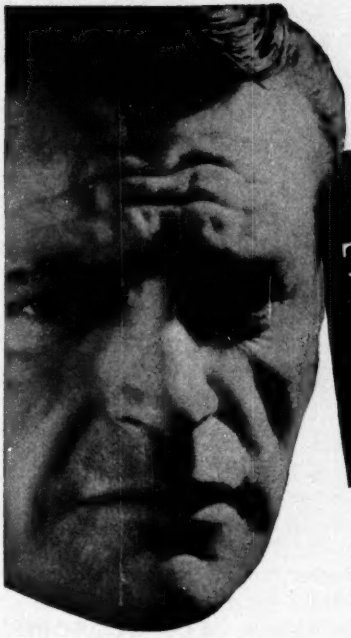

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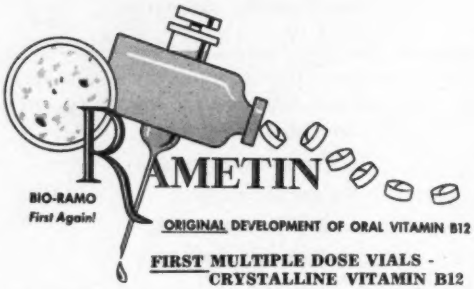

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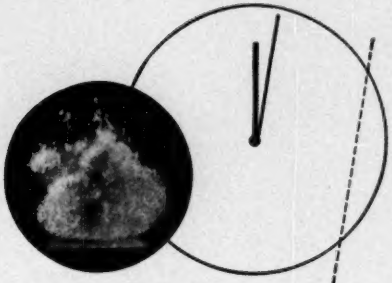

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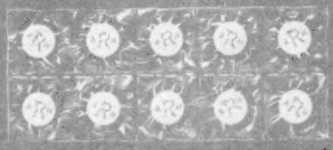

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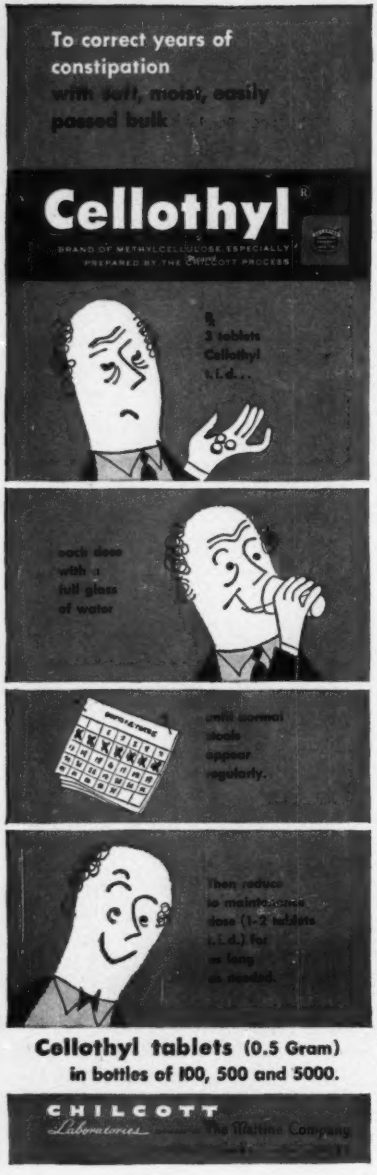
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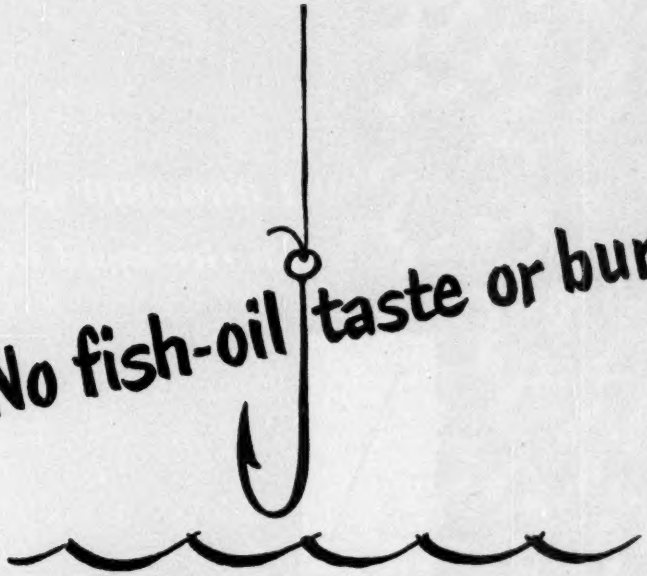

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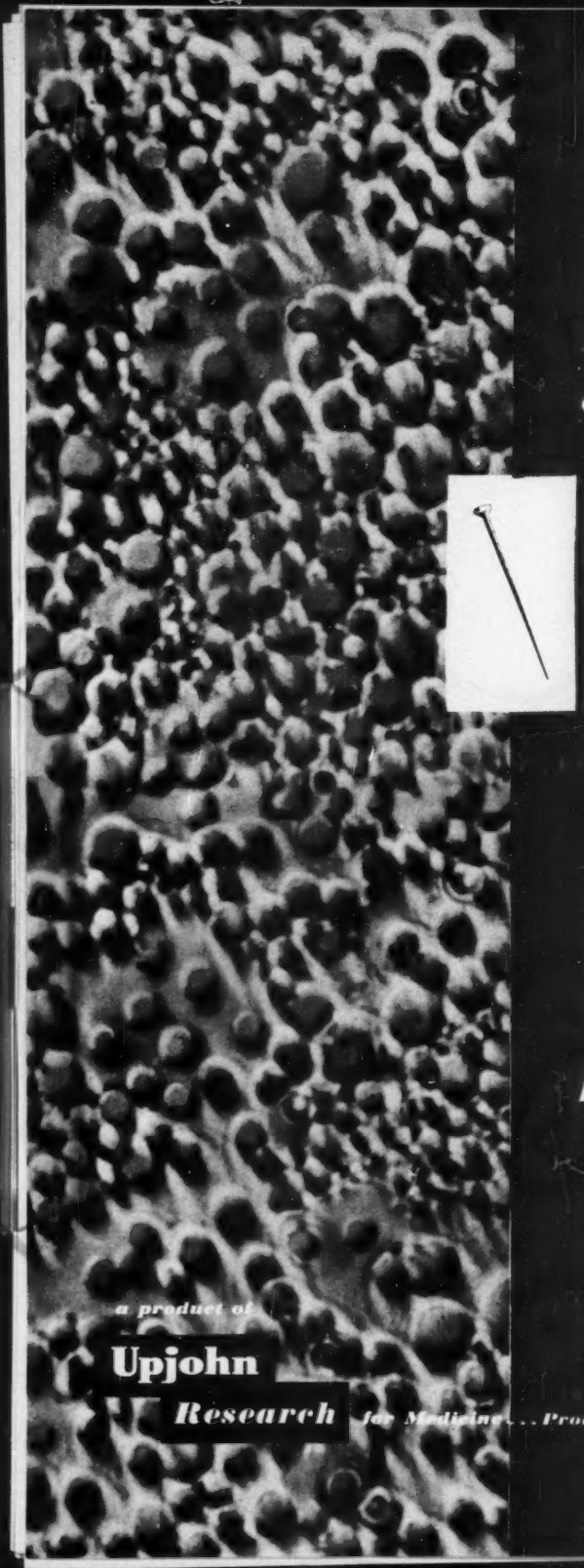

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THE CAUSE OF FAT NECROSIS FOLLOWING EXCISION OF THE PANCREATIC DUCT FROM THE DUODENUM

H. L. POPPER AND H. NECHELES, Chicago, Illinois.

IN PREVIOUS papers (1-4) the effects of various experimental injuries to the pancreas were reported. Transverse or lengthwise section of the pancreatic duct was followed by intraperitoneal fat necrosis only when the animals has been fed before or after the operation, or when cholinergic drugs had been given postoperatively (1). However, extensive crushing or complete transverse tearing of the pancreas did not produce fat necrosis, whether the animals were fed or starved pre- and postoperatively (2). In the starved dogs with section of the duct and in the fed and starved animals with crushing or tearing injuries of the pancreas, the wounds of this organ were found to be covered by firmly adherent omentum or occasionally by a firmly adherent loop of small bowel. This showed that, following trauma of the pancreas, sealing of opened ducts or of wounds by omentum takes place, which obviously is possible only if pancreatic secretion, which would prevent the sealing of such wounds, is absent. Pavlov (5) has found that, following trauma of the pancreas, suppression of its secretion occurred, which seemed to be proportional to the degree of injury. We believe that these observations of Pavlov can explain some of the results of our experiments. Thus in severe injuries, such as crushing or tearing of the gland, inhibition of pancreatic secretion appeared to be profound, resisting stimulation by pre- or postoperative feeding and even by large intravenous doses of secretin administered following traumatization of the pancreas (3). The presence in the peritoneal cavity of moderate amounts of blood or bile, or of necrotic omentum, or even ischemic necrosis of part of the pancreas, had no demonstrable effect on the healing process of injuries of the pancreas (3).

While mere section of the ducts and crushing or tearing of the gland did not produce fat necrosis, excision of the pancreatic duct from the duodenum with an attached piece of duodenal mucosa (E. D. M.) led almost consistently to very pronounced changes (4). Of 20 dogs, which were starved before and after the operation, 16 died between the 2nd and 8th postoperative day with extensive intra-abdominal and intrathoracic fat necrosis. The remaining 4 dogs were sacrificed on the 3rd, 4th, 8th, and 18th day respectively.* Three had no intraperitoneal pathology and one revealed a moderate amount of disseminated fat necrosis.

Thus, fatal fat necrosis occurred in 80% of these animals which is in sharp contrast to the few and insignificant findings following other pancreatic injuries in starved dogs mentioned above. The fact that duodenal mucosa was excised with the pancreatic duct was the main difference from the previous experiments and was probably responsible for the pathologic findings. Pancreatic trypsinogen is activated by contact with duodenal mucosa. Thus, activated pancreatic juice draining into the peritoneal cavity was the possible cause of fat necrosis. However, our previous results (1), where diffuse fat necrosis developed in fed animals following simple section of the pancreatic duct speak against this assumption. In these experiments the pancreatic juice did not come in contact with duodenal mucosa, and yet it caused extensive pathology. Also, pancreatic trypsin is activated by blood, by necrotic tissue and possibly by bile, and yet experiments where such combinations were tried, yielded negative results.

The duodenum of the dog contains a mixed flora of bacteria, and the observed pathologic changes could have been due to the combination of pancreatic injury and bacterial infection. Thus, a local bacterial peritonitis might have prevented the sealing of the pancreatic injury, permitting the pathologic process to spread. With this possibility in mind, care was taken to avoid bacterial contamination, and daily injections of penicillin and streptomycin were given.

Bacteriologic studies of the peritoneal fluid of several dogs of this group (E.D.M.) were performed. In 2 dogs with extensive fat necrosis, cultures were sterile. A mixture of various pathogenic bacteria was found in one dog with generalized fat necrosis and in 2 of 3 animals which did not develop any fat necrosis. This suggests that bacterial contamination did not play a decisive role in the development of fat necrosis.

The production of fat necrosis in the E.D.M. experiments can be explained by the observation that the musculature, but not the mucosa, of the duodenal flap contracted. This transformed the excised duct into a small, mushroom-like structure, covered by overhanging mucosa, which did not leave traumatized muscle tissue exposed. The duodenal mucosa, in contrast to the pancreas, does not appear to be subject to post-traumatic secretory inhibition, continuing to secrete juice as well as mucus, which appear to prohibit the formation of adhesions. Thus, if a firm adhesion cannot occur by the time the pancreas has recovered from its secretory inhibition, pancreatic juice will drain freely into the peritoneal cavity with subsequent development of fat necrosis.

In fact, in all dogs with extensive fat necrosis, the duodenal flap was shown to be free, i.e., not covered by any adherent tissue, while in 3 dogs without fat necrosis and in one dog with moderate non-fatal fat necrosis, the duodenal flap was covered by firmly adherent omentum or by a loop of intestine. These experiments demonstrate that fatal fat necrosis developed only if the cut pancreas duct remained open and was not sealed by adhesions, which would have prevented spilling of pancreatic juice. The following experiments

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*Two moribund dogs are included which were sacrificed on the 3rd and 4th postoperative days respectively.

Submitted April 11, 1951.

were performed on starved dogs to study the validity of this explanation.

EXPERIMENTS

In 3 dogs the pancreatic duct, together with a piece of duodenum, was excised as described above, but an incision was made through the papilla, the duodenal flap, and the pancreatic duct. The animals were sacrificed on the 22nd, 25th, and 29th postoperative day respectively. In all 3 dogs omentum was found so densely adherent to the pancreas, that the duodenal flap could not be identified. One dog showed a moderate amount of fat necrosis but the other 2 did not show any.

In 3 dogs, 2 separate procedures were performed. The pancreatic duct was transsected close to the duodenum and left open. A piece of the wall of the duodenum with intact blood supply was excised, the duodenum was closed, and the duodenal flap was left free, close to the open pancreatic duct. One animal was sacrificed on the 3rd and the other two on the 7th postoperative day. Autopsy did not reveal fat necrosis in any of these dogs. The pancreatic duct was plugged by adherent omentum in 2 dogs, and by a loop of small bowel in the 3rd one. The duodenal flap was found to be free in 2 dogs and covered by firmly adherent omentum in one dog.

In 3 dogs, the duodenal flap was buried in a furrow formed in the pancreas with the help of two sutures, one above and one below the pancreatic duct. In order to avoid obstruction to the flow of pancreatic secretion, the sutures were tied loosely so that the open pancreatic duct remained patent, and the duodenal flap remained visible and easily accessible. Sacrificed on the 4th postoperative day, the dogs did not show any fat necrosis. In one dog, a portion of the duodenal wall and in 2 dogs, omentum was firmly adherent to the portion of the pancreas which surrounded the inverted duodenal flap and the orifice of the pancreatic duct, thus sealing them off completely.

DISCUSSION

Our previous experiments have demonstrated that, following injuries to the pancreas, fat necrosis develops under the following conditions: following sectioning of the main pancreatic duct, the development of fat necrosis depends entirely upon the presence or absence of stimulation of pancreatic secretion. In the first case, fat necrosis develops in most animals; in the second case, the opened duct is covered by adhesions and fat necrosis does not develop. In the case of severe trauma to the pancreas, its external secretion is depressed. Mere section of the main pancreatic duct does not seem to constitute a severe trauma, and the gland continues to respond to stimulation. Crushing and tearing of the pancreas constitutes severe trauma, and external secretion of the gland appears to be suppressed, and not responsive to stimulation for a prolonged period of time. Thus, the traumatized parts of the pancreas are covered by adhesions, and fat necrosis does not develop, even when stimulation of pancreatic secretion has been attempted.

Excision of the main pancreatic duct from the duodenum, together with a piece of duodenum attached to it, leads to fat necrosis. The operative trauma does not appear to be severe enough to suppress pancreatic secretion, and the latter enters the peritoneal cavity freely. The present series of experiments demonstrates that fat necrosis in these animals is due to the prevention of formation of adhesions. This is proved by the following experimental findings: when the piece of duodenal mucosa and the attached pancreatic duct were split open, or when a piece of mucosa and the sectioned duct were separated and left in the abdomen, or when the piece of mucosa at the end of the pancreatic duct was inverted into the pancreas, firm adhesions formed, and fat necrosis was absent. The chance for activation of pancreatic enzymes was present in these experiments. However, a wound surface was created, which made adhesions possible. In the experiments in which the duct, together with a piece of mucosa, was excised from the duodenum, a traumatized surface was not present. The excised piece of duodenal muscle contracted, while its mucus membrane relaxed, forming a mushroom-shaped cover over the edges of the cut muscle, thus not leaving traumatized tissue exposed. A further factor favoring the appearance of fat necrosis were the secretions of the duodenal flap, which prevented adhesions from forming.

SUMMARY

Excision of the pancreatic duct from the duodenum, together with a piece of duodenum attached to it, and leaving this structure freely open in the abdomen, leads to fat necrosis. The fat necrosis is not due to activation of pancreatic enzymes in the abdomen, but it is due to the successful prevention of the formation of adhesions between omentum or bowel and the flap of duodenal mucosa attached to the duct. The reasons for the prevention of the formation of adhesions are the secretion of mucus and of enteric fluid by the flap of duodenal mucosa and the formation of a cap of mucosa over the contracted piece of duodenal muscle. The latter covers the edges of the duodenal musculature and thus covers a traumatized area, which otherwise would predispose to formation of adhesions. Experiments in which the pancreatic duct with the attached piece of duodenal mucosa was traumatized in such a way as to produce conditions favoring formation of adhesion, proved this point.

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HEALING OF PEPTIC ULCER

MAURICE FELDMAN, M. D.* AND TOBIAS WEINBERG, M. D.** Baltimore, Maryland.

OUR INTEREST in this subject was stimulated by the fact that there exists a definite disparity between the number of healed ulcers found at autopsy and the healing of ulcers observed in clinical and roentgenologic studies. How often do peptic ulcers heal, is a question frequently asked which cannot be unequivocally answered. It has been a matter of general opinion, however, that most peptic ulcers heal spontaneously. It has been asserted by some and disputed by others that the incidence of healing of peptic ulcers is exceedingly high. The true incidence of healing of peptic ulcers has by no means been studied exhaustively. There is an obvious disparity in the incidence of healing as recognized clinically, roentgenologically, gastroscopically, and at autopsy. This is no doubt attributable to the difficulty in securing definitive information necessary to establish the presence of healing. There is also an astonishing paucity of literature concerning this subject. One of the great difficulties in the determination of healing of peptic ulcers is the fact that the healing of an ulcer may be so complete that no visible or gross evidence of an ulceration can be detected. On the other hand, there may be demonstrable evidence as shown by scarring, pitting, thickening, and other signs, such as adhesions. The clinical and roentgenologic evidence of healing of peptic ulcer is a common observation. However, there is a great discrepancy between clinical healing and that observed roentgenologically. The presence of healed ulcers may be definitely observed in surgical and autopsy specimens. Clinically, one sees many cases of apparent and real healing of peptic ulcers.

There seemed to be a compelling need for definitive studies on the healing of peptic ulcer. Interest in this problem was motivated by a perusal of the autopsy records of the Sinai Hospital. A survey was made of this material in the belief that it might afford some index as to the incidence of healing of peptic ulcer. This study was undertaken to determine how often peptic ulcers heal. Although, as previously stated, the occurrence of healed peptic ulcers is a common clinical observation, we have found that apparently it is an infrequent observation among autopsy material. A study was made of 1,082 adult autopsies. Among these we found fifty-four cases of active chronic peptic ulcers, and eighteen cases which were completely healed. Of the fifty-four active ulcers, twenty-nine were duodenal, twenty were gastric, and in five instances there was both a duodenal and a gastric ulceration. The incidence of active peptic ulceration among these autopsies was 5 per cent.

It is well recognized that healing of peptic ulcers is difficult to detect in the gross examination of autopsy material because of the frequency of complete healing and epithelialization of the mucosal ulcer surface during the lifetime of the patient. However, it was thought that a careful and minute study of the autopsy material might aid in establishing the incidence of healing ulcers. There has been little statistical data concerning this phase of the ulcer problem. It would seem apparent from our autopsy study that the incidence of complete healing of peptic ulceration is rather low. The incidence of healed ulcers encountered in our 1,082 autopsies was 1.7 per cent. Of the eighteen cases of completely healed ulcers, five were gastric and thirteen were duodenal.

It is important to emphasize again that it is extremely difficult to detect evidence of completely healed ulcers, especially those which were rather small. The re-epithelialization of the mucous membrane over the healed ulcer area often leaves slight surface evidence of the ulceration. This no doubt often accounts for the many cases of healed ulcers which are not recognized at autopsy.

The healing of peptic ulceration is shown at autopsy by a number of lesions: (1) Stellate scars. (2) Dimples or depressions. (3) Thickening in the old ulcerated area. The thickened tissue is palpated, especially in the healed penetrating type of ulceration and when the serosa is involved. (4) Transillumination. The opened stomach is spread over a light and the healed ulcer is shown as a small area of opacity produced by the localized thickened tissue. This latter method of examination has been recommended by Bolton and reemphasized by Ivy et al. The most important procedure to determine the presence of healing of a peptic ulcer is by microscopic examination. Histologically, the healed peptic ulcer area shows a thinning of the mucosa, the result of a sparse and irregular regeneration of glandular elements in a dense connective tissue. The glands are of the undifferentiated or mucoid type usually. The muscularis mucosa does not regenerate. In those ulcers in which the muscularis has been partially destroyed and in which healing has taken place, the destroyed portion of the muscle is replaced by fibrous tissue.

Clinical healing of a peptic ulcer cannot be accepted as true evidence of healing in all cases. At times it is impossible to determine clinically whether or not an ulcer has healed completely. The fact that a patient may be asymptomatic over a varying period of time does not indicate in all instances that the ulcer has healed. Numerous examples of cases of symptom free ulcers are noted during roentgenologic studies which show evidence of active ulceration with a niche type of filling defect, but still reveal few symptoms denoting activity of the ulcer. Because of the frequent remissions of the symptoms common to peptic ulcer it is extremely difficult to be certain that healing has taken place, at least from a clinical standpoint. One of the most important revealing evidences of possible healing of a peptic ulcer is the disappearance of blood in the stools. A persistent absence of blood, with stool specimens examined over a period of weeks, is commonly believed to be indicative of healing. However, even this finding may not be a sign of certainty of healing.

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This has often been shown by comparing the roentgenologic evidence of activity with the findings of stool examinations. It is not unusual to find an absence of blood in the stools, yet on roentgen examination an ulcer niche, a sign of activity, is clearly demonstrated.

The gastroscopic examination is one of the most accurate objective visible means of determining the presence of healing of a peptic ulcer. The incidence of healing ulcers has not been established by this type of examination. Furthermore, this method presents many disadvantages and surely cannot present the true incidence because (1) all ulcers are not observed under the gastroscope, (2) many stomach ulcers are not accessible, (3) duodenal ulcers cannot be demonstrated, (4) it is difficult to obtain routine gastroscopic examinations, and (5) the necessity for repeated examinations would mitigate against this procedure.

The roentgenologic method of examination seems to be the most practical procedure to determine the healing of an ulcer. The ulcer niche can be observed carefully at frequent intervals and its disappearance determined with great accuracy. It must be pointed out here, however, that the disappearance of the ulcer niche defect as shown roentgenologically often occurs before complete healing has taken place.

Numerous factors must be considered in the healing of peptic ulceration. These are: (1) the size and depth of the ulcer, (2) duration of the ulcer, (3) the circulatory changes in the ulcerated area, (4) age of the patient, (5) associated conditions, and (6) complications. The size of the ulcer if superficial is not an important factor. Large superficial ulcers may heal rapidly without producing any gross changes. Ivy et al. point out that there is no correlation between the size of the ulcer crater and the rate of healing time. The depth of the ulcer crater is probably the most essential factor in the time of healing and the production of scarring. The time of healing of a peptic ulcer is variable. The acute ulcers seem to heal rapidly. These are more likely to be superficial and produce little if any detectable scarring. The usual time required for complete healing, as demonstrated by the roentgen method, varies from two to eight weeks. In some instances many months may elapse, whereas in others complete healing never occurs. Cummins et al. studied the healing time roentgenologically in sixty-nine cases of peptic ulcer and found the average healing time in sixty-three cases of duodenal ulcer was thirty-seven days; in six cases of gastric ulcer the average healing time was forty-two days. Besides the roentgen evidence of healing they also utilized evidence of absence of occult blood as part of their criteria in the determination of healing of the ulcer.

COMMENT

There is an obvious discrepancy between the clinical and autopsy incidence of the healing of peptic ulcer. According to Stewart, Bockus, Feldman, and others, a conservative estimate of the incidence of peptic ulcer in the general population is about 10 per cent. In the present autopsy study of 1,082 consecutive adult necropsies, with fifty-four active and eighteen healed ulcers, there was a total incidence of 6.7 per cent. It appears that since only 1.7 per cent of these were completely healed, the incidence of healing of peptic ulceration as shown by our autopsy studies is unusually low, and the disparity between the clinical and autopsy material is statistically highly significant.

SUMMARY

The clinical and roentgenological healing of a peptic ulcer is a common observation. On the other hand, healed peptic ulcers are not as frequently observed in a study of autopsy material. The autopsy incidence of healed peptic ulcer was 1.7 per cent. The great disparity in the incidence of healing between the clinical and necropsy findings is probably attributable to the completeness of the healing and re-epithelialization of the mucosa, so that grossly many of the healed peptic ulcers cannot be demonstrated.

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THE HEALING OF A PRIMARY DUODENAL ULCER WITH THE LATER DEVELOPMENT OF A GASTRIC ULCER

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THERE are abundant references in the literature regarding the development of recurrent peptic ulcer, but the impression is gained that these recurrences are due to the original ulcer. However, scant information is available relating to peptic ulcers occurring at a new site following the healing of the original ulcer. From a study of our records, it would appear that the latter condition occurs perhaps more frequently than has been suspected. Instances of the occurrence of a new

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peptic ulcer at different sites have not been sufficiently stressed.

This study embraces a series of 500 cases of peptic ulcer. Of these, 458 or 91.6 percent were duodenal ulcers, 21 or 4.2 percent were gastric ulcers, and in 21 or 4.2 percent there were combined gastric and duodenal ulcers. In this presentation we are particularly interested in the healing of an ulcer in the duodenum with the development of a new ulceration in the stomach. Interest in this study was stimulated by our experience with a small group of patients in whom a new peptic ulcer had developed at a different site after the original ulcer had completely healed. The purpose of this paper, therefore, is to point out and re-emphasize that recurrent episodes of symptoms in cases of peptic ulcer may not always be due to the original ulcer, which may have been healed for a long period of time, but that a new ulcer had formed elsewhere. The formation of a new peptic ulcer at a different site than the original ulcer is not often suspected and it is this concept that has focused our interest on the topic of the healing and activity of combined peptic ulcers.

There can be no question that peptic ulcers occur together frequently, even though they may not be recognized singly or separately by clinical and roentgenological methods of examination. It is not uncommon to find at operation or at necropsy, combined and multiple ulcerations when on roentgen and clinical studies only a single ulcer was detected. There have been numerous cases of combined gastric and duodenal ulcers reported in the literature, but the problem of multiple or actively combined ulcerations will not be discussed in this communication. Rather, it is our desire to report here, on the development of a new ulcer, at a different site, after the original one had apparently completely healed as evidenced by clinical and roentgenologic examinations. It must be admitted, however, that in those instances in which two ulcers are present there is no reason to suspect that they appeared simultaneously in all cases.

How often does a secondary ulcer occur after the primary ulcer had healed is another question which we have attempted to answer. Up to this time no one has established this incidence. In a perusal of the literature, only casual reference is made to the formation of a new peptic ulcer with the healing of an old one at a different site. In a survey of records of 1,131 autopsies* we found only 6 cases or 0.53 percent of combined gastric and duodenal ulcers, in none of which did we encounter a single instance of a completely healed duodenal ulcer associated with an active gastric ulcer. In our clinical study of 500 cases of peptic ulcer we found 21 cases or 4.2 percent with combined gastric and duodenal ulcers. It would appear, therefore, that about one in 25 ulcer patients in this series presented a combined gastric and duodenal ulcer. These ulcers were demonstrated by clinical and roentgenological study, a finding which cannot be borne out at postmortem examination. Furthermore, it becomes clear that the subject of a new ulcer is also a clinical-roentgenological one and not one to be studied with necropsy material. Of the 21 cases of combined gastric and duodenal ulcers, 15 showed both ulcers to be active and 6 revealed roentgen and clinical evidence of a completely healed duodenal ulcer with an active gastric ulcer. In these six cases, the original ulcer appeared in the duodenal bulb, which had later healed; the secondary peptic ulcer was noted in the pylorus, close to the sphincter, in 5 cases and in one case the ulcer was found on the posterior wall of the antrum of the stomach.

The recurrence of peptic ulcer symptoms in a patient whose ulcer had been known to have been completely healed, should be a signal to explore the possibility of the formation of a new ulcer as well as to consider a recurrence of the old one. It is well known that peptic ulcer is characterized by a high recurrence rate, but the problem presented here is the recurrence of peptic ulcer symptoms after the original ulcer had completely healed with the formation of a new ulcer at a new site. In the study of combined peptic ulcers the question often arises as to whether one of the ulcers is healed at the time both are found, or whether both are active. In some instances one of the ulcers may be active and the other healed or inactive. Of the 6 cases which revealed healing of one of the ulcers, the original ulcer had occurred in the duodenal bulb, and after it had been healed for a considerable period of time, there later developed a gastric ulcer. The time interval between the healing of the original peptic ulcer and the formation of the new ulcer at a different site varies. In our 6 cases the lapse of time between the formation and recognition of the old and new ulcer ranged from one to twenty-seven years. In one case the interval of time between the occurrence of the second ulcer was one year, in 3 cases ten years, in one case sixteen years, and in one case twenty-seven years. All of these cases were studied over a period ranging from 5 to 30 years. They had been asymptomatic with evidence of complete healing and had been re-checked periodically with roentgen studies. During the intervals between periodic examinations the roentgen and clinical pictures were those usually observed in cases of healed peptic ulcers, i.e. free of symptoms, disappearance of the ulcer niche, absence of irritability of the duodenal bulb, elimination of localized tenderness, and disappearance of blood from the stools. At no time after the original ulcer had healed was there any evidence of occult bleeding, but following the recurrence of symptoms as a result of the formation of a new ulcer, occult bleeding was again noted in the stools.

The clinical symptomatology so far as the patient can relate is not usually indicative of the formation of a new ulcer. Often there is no change in the gastric acidity values. It therefore appears that without the x-ray studies one can rarely determine the exact site of the active ulcer, and thus the roentgen examination is the deciding factor in locating whether the ulcer is on the gastric or duodenal side of the pylorus. Clinically, it must be admitted that it is very difficult to determine whether a second ulcer had developed at a new site. Obviously, one too often concluded clinically that the old ulcer had recurred. The continuance of ulcer symptoms, however, does not necessarily indicate the development of a new ulcer. As an example, a complication such as a prolapse of the gastric mucosa into the duodenal bulb may be the reason for the persistence and recurrence of symptoms. Moreover, in our series

*This autopsy material was obtained from the records of the Sinai Hospital, through the courtesy of Dr. Tobias Weinberg, Director of Laboratories.

of peptic ulcer cases we not infrequently found two ulcers when only one could be diagnosed clinically. An example of a typical case of a completely healed duodenal ulcer with the development of a new gastric ulcer is described below.

CASE REPORT

Male, aged 41, consulted us first in 1924, with a clinical history of a duodenal ulcer, which was verified by an x-ray study, showing an active ulceration. He responded well to treatment, but has had periodic intervals of exacerbations and remissions with a recurrence of his duodenal ulcer niche in 1940. Following appropriate therapy he again became asymptomatic and roentgen studies revealed a disappearance of the ulcer niche defect. Periodic examinations since then continued to show an absence of the ulcer niche. In 1943, another check-up examination still revealed complete healing of the ulcer. The patient had been entirely free of all symptoms until 1950, when he developed a symptomatology which differed somewhat from his original ulcer pattern in that the symptoms were more severe, persistent and lasted longer. In addition, he had for the first time complained of vomiting. Although frequent roentgen studies prior to this latter episode revealed a healed duodenal ulcer, an x-ray study made at the later date still showed the healed duodenal ulcer, but in addition there was an unsuspected ulcer located in the stomach near the pyloric ring. During this episode, the stool examinations revealed evidence of occult blood. One month later, upon re-examination, the pyloric ulcer had healed with disappearance of symptoms, the stools were free of occult blood, and there was a disappearance of the ulcer niche filling defect in the roentgen examination. The patient's gastric acidity, when his duodenal ulcer was active showed a total acidity of 82 and free HCl of 52. When his gastric ulcer appeared, the total acidity was 36 and free HCl 15.

COMMENT

In this case, there was a clear-cut history, confirmed by x-ray studies, of an active duodenal ulceration, which later showed evidence of complete healing. After a lapse of ten years, there developed a gastric ulcer near the pyloric ring, with a change in symptomatology and gastric acidity. However, in most of our cases there was no distinct change in symptoms or gastric acidity values.

SUMMARY

In a study of 500 cases of peptic ulcer, a combined gastric and duodenal ulcer was found in 21 cases or 4.2 percent. Among the 21 cases of combined peptic ulcers, there were 6 instances or 1.2 percent of the entire series or 28.5 percent of the combined ulcers, in which it was clinically and roentgenologically demonstrated that one of the ulcers had been healed completely and the other had remained active. The site of the original ulceration was in the duodenum, and the second ulcer occurred in the stomach. Attention is drawn to the fact that one must not always assume that when there is a recurrence of symptoms it is due to a recurrence of the same ulcer at the original site. It is further emphasized that when a patient is found to have a peptic ulcer which has shown roentgen and clincial evidence of complete healing and the patient has been asymptomatic for an indeterminate period of time, the recurrence of digestive symptoms may indicate the formation of a new ulcer at a different site. A clinical example of the latter type of case is described.

THE EFFECT OF CHLORIDE CONCENTRATION IN THE DETERMINATION OF LYSOZYME ACTIVITY

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IN THE study of the lytic activity present in gastric juice (1) it was found that chloride concentration influenced the activity of lysozyme sufficiently to affect the ultimate results of its determination as developed by Smolelis and Hartsell (2). The modification necessitated by this condition will be described.

Since Fleming (3) discovered the lytic activity of lysozyme on cultures of *Micrococcus lysodeikticus*, various measures have been developed for assaying its activity. The method of Sandow (4), Goldsworthy and Florev (5) was based on the clearing of cell suspensions of *Micrococcus lysodeikticus* with known concentrations of lysozyme.

Later, microscopic observations of lytic activity were made by Rosenthal and Lieberman (6). A technique developed by Boasson (7) employed the use of a Mall extinctiometer in conjunction with known standards, the comparisons giving the amount of lysozyme present as a direct relationship of its activity.

Modifications of these various determinations were developed. However, the latest and quantitative determination of lysozyme was developed by Smolelis and Hartsell. The accuracy of their method was enhanced by the use of crystalline lysozyme (8). Briefly their method is as follows:

Micrococcus lysodeikticus (Fleming ATCC 4698) is obtained from 18 hour subcultures by harvesting in phosphate buffer. The bacteria are then exposed to ultra violet light, shell frozen and dried in vacuum.* In use, the organisms are suspended in phosphate buffer (M/15 at pH 6.2). The suspension is adjusted spectrophotometrically to give 10% transmission at 540 mμ wave length. The blank used in the assay is the same phosphate buffer employed in the preparation of the suspension and standards.

The standards are a serial dilution of crystalline lysozyme ranging from .00015 mg to 0.005 mg of lysozyme per ml. 5 ml of the bacterial suspension is added to 5 ml of the standards and unknowns. These are then left to incubate 20 minutes at room temperature, after which their respective transmittances are read.

Smolelis and Hartsell found their method quantitatively reliable in working with animal extracts (e.g. rat kidneys), rehydrated and fresh egg albumin.

While employing this method in determining the lytic

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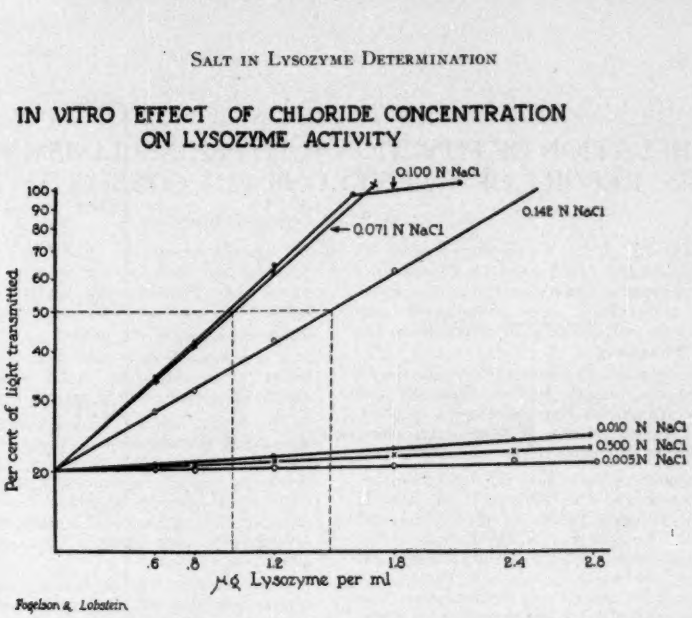
*The dried substrate organism for our experiments is donated by Difco Laboratories, Detroit, Michigan.



Graph 1: Typical standard lysozyme curves showing the effect of varying chloride concentrations on lysozyme activity. The numbers on each line indicate normality of NaCl in the phosphate buffer solution.

activity of gastric juice, we found that the standard curves varied considerably according to the salt concentration present in the buffer. A very low salt concentration, and a high one seems to inactivate lysozyme, a salt concentration of 0.071 N NaCl to 0.100 N NaCl giving consistently optimum lytic activity. It therefore is important to have equal salt concentration in the standard curve and in the unknown solutions in order to be able to use the standard curve for a particular unknown. This was achieved by the addition of NaCl to the buffer to make a 0.071 N NaCl solution. The improved Chloride-Phosphate buffer is now used in all Lysozyme determinations (9) and the results obtained have been reliable, consistent and applicable for high and low lytic activities. Although the modification is slight its importance is graphically illustrated.

SUMMARY

The phosphate buffer used in the determination of lysozyme by the method of Smolelis and Hartsell was modified by the addition of a given concentration of NaCl. This change was shown necessary in determining the lytic activity present in gastric juice, when it was observed that very low as well as high chloride concentrations in the buffer solution alter lysozyme activity considerably.

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ON THE RELATION OF FUNCTIONAL HYPERINSULINISM TO VISCEROPTOSIS: REPORT OF TWENTY-ONE (21) CONSECUTIVE CASES

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VISCEROPTOSIS AND Cardioptosis were described by Glenard (1885) and by Cherchevsky (1887). The mechanisms which give rise to the cardiac symptoms of visceroptosis were investigated anatomically by Keith and clinically by Wenkebach, my late teacher in Strassburg.

Clinically, visceroptosis manifests itself, besides the digestive disturbances, mainly by neurovascular and neurovegetative symptoms. This paper seeks to prove that there is a causal relation between visceroptosis and hyperinsulinism in various forms and degrees.

A brief description of the anatomical connections between the pancreas and the duodenum will help to comprehend the etiological relation of visceroptosis and hyperinsulinism. The pancreas is about eight inches long and lies transversely on the posterior abdominal wall; its greater part behind the stomach. The head of the pancreas lies in the concavity of the duodenum. The body of the organ crosses to the left in front of the vertebral column, the left kidney and the suprarenal gland. The tail touches the visceral surface of the spleen. The pancreas is connected with the duodenum through the pancreatic duct and the accessory pancreatic duct. Arteries: (1) The superior pancreatico-duodenal; (2) The inferior pancreatico-duodenal. Veins: (1) The pancreatico-duodenal veins of which some pass downward and to the left, on the front of the head to join the superior mesenteric. Other veins cross the back of the head and open into the superior mesenteric or the portal vein. Several small pancreatic veins join the splenic. In visceroptosis the stomach and the duodenum are often found in the pelvis.

It is reasonable to assume that the varying displacements of the duodenum causes twisting of the pancreatico-duodenal veins in various degrees.

This in turn produces a venous-stasis in the pancreas, stimulating this organ to more than normal activity in its internal secretions, the resulting hyperinsulinism producing hypoglycemia and irregularities of the blood-sugar level, especially after moderate exertion or after digestion. If visceroptosis is sufficiently pronounced, hypoglycemia may obtain even in fasting or in the absence of exertion.

After wearing the support, and frequent meals to correct hypoglycemia, patients gained weight and reported being free of nervous symptoms and to use one of the patients' own words, "free of indescribable suffering, for the first time in 30 years."

Case No. 6 had, through a misunderstanding, a fasting blood sugar taken only. I included it in the list because it was a consecutive case and showed fasting hypoglycemia.

In age, the 21 cases range from 15 to 60. Eleven cases are under 30 years of age. The lowest blood sugar observed was Case No. 2 who had 36 mg in the second hour and Case No. 8 who had 31 mg in the second

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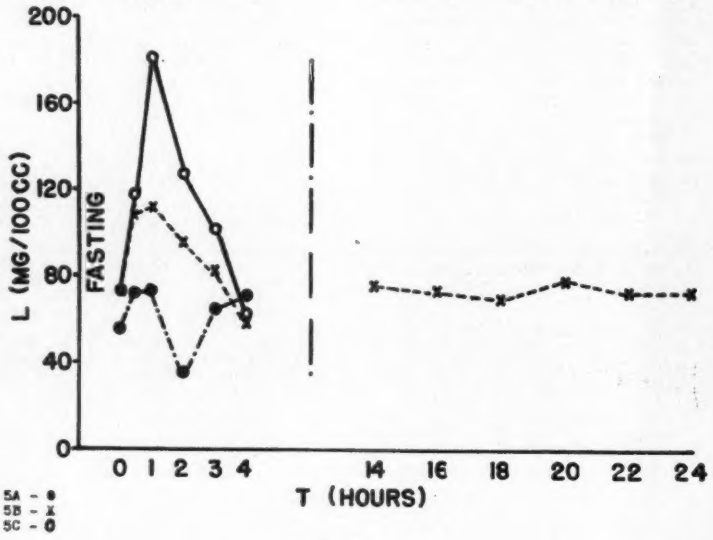

Figure 1

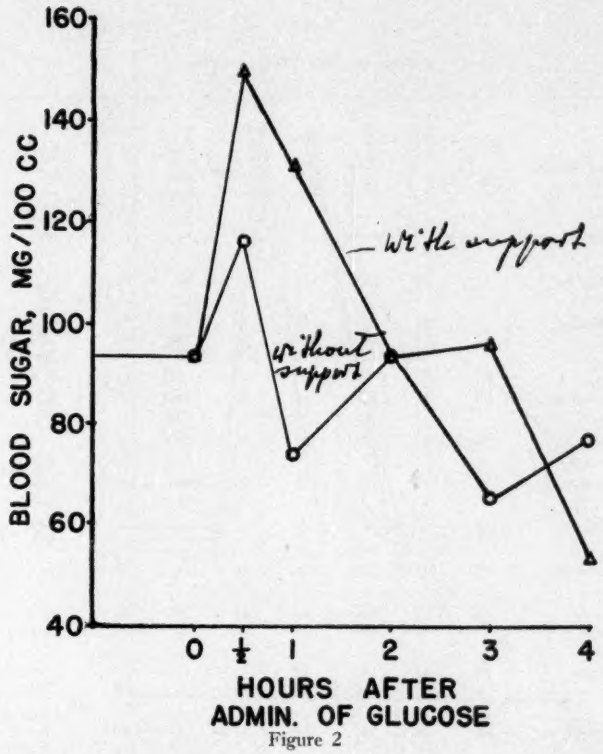

Figure 2

hour. Case No. 5 is interesting because it shows how a little walk caused the sudden drop of the blood sugar from 177 mg to 80 mg.

Case No. 17 merits special attention. I first observed the syndrome in Mr. J. R. in July, 1944. A glucose tolerance test was taken at that time in Mt. Sinai Hospital but the records were lost when the patient moved to another city. It was only on Feb. 22, 1951 that I had occasion to re-examine this patient at Mt. Sinai Hospital after seven years with identical results. In this case, the blood sugar level after ingestion of 100 grams of dextrose was in all tests, except one, (in the second hour) below the fasting level of 90 mg.

Graphs were made from three cases. Graph No. 1 (Case No. 2) is a composite graph representing blood sugar levels under three different conditions: (A) under ambulatory, without support; (B) recumbent in hospital; (C) ambulatory, with support.

Graph No. 2 (Case No. 9) is a composite of two graphs: (A) taken with support (was wearing support for two years); (B) eleven months later removed the support while taking the test.

Graph No. 3 is a composite of cases: No. 1, 3, 4 and 5 and can be easily identified through their respective charts.

Cases No. 3 and No. 9 had experience in wearing the supports from one to two years respectively, before the test.

As evident from the chart, Case No. 8 had also taken the glucose tolerance test again with support. This patient is 6'5" tall; he wore his support for only a few weeks over the pelvic region which did not correct the visceroptosis. He only converted it into another variety of visceroptosis.

Case No. 20 wore the support only one day before he took the second test and did not know how to apply it properly.

Cases No. 8 and No. 20 are, nevertheless, instructive as they show how the pancreas functions change under different conditions. Some of the patients told me they actually felt it (in the head) when the blood sugar level changed during the 4-hour glucose tolerance test. To correct visceroptosis and hyperinsulinism, it is not enough to prescribe an abdominal support as almost each patient has to be fitted under the fluoroscope and the garment must often be altered in order to make the correction required. The patient must be instructed in the proper application of it.

In this connection, a quotation from Sajour (*Analytical Encyclopedia of Practical Medicine*, Vol. 5, 771, 1922) is interesting:

"Visceroptosis is such a common condition that it furnishes the strongest argument for routine physical examination, both of the chest and the abdomen. It is not at all unusual for an individual to pass through numerous hands, medical and even surgical, without the true nature of the condition being dis-

TABLE I

4-HOUR GLUCOSE TOLERANCE TEST

Date	Name of Patient	Age	MG/100cc FASTING	MG/100cc ½ HR.	MG/100cc 1 HR.	MG/100cc 2 HRS.	MG/100cc 3 HRS.	MG/100cc 4 HRS.	REMARKS
No. 1									
7-1946	Stanley Novitsky	45	98	173	112	86	61	86	
No. 2									
3-3-1950	Edward Kraus		37	72	74	36	65	72	Second test (middle row) taken month after first
3-27-1950		48	74	109	112	96	83	59	Patient was lying down during
1-23-1951			74	158	182	127	102	63	second test.
No. 3									
6-23-1950	Dan O'Laughlin	26	85	116	110	89	88	95	
No. 4									
8-3-1950	Ben Gershowitz	26	86	165	172	92	69	66	
No. 5									Patient took a walk between the
8-8-1950	Miss G. Lebowitz	24	87	179	177	80	125	105	first and second hour.
No. 6									
8-11-1950	Henry Bildstein	18	68	—	—	—	—	—	Patient did not complete test.
No. 7									
8-29-1950	Earl Merriman	30	114	155	140	86	70	90	
No. 8									
9-13-1950	Max Saewitz	19	74	139	86	45	39	56	6'5''—wore support over pelvic
3-27-1951			87	125	71	46	31	78	region only.
No. 9									
1-18-1950	Harold Stein	26	93	117	74	93	65	77	Without support.
11-1-1950			94	150	132	95	95	53	With support.
No. 10									Patient has worn pelvic support
10-29-1950	Ralph Thiesse	22	96.1	123	108	87.3	79	80.6	for 2 yrs., but did not wear it during test.
No. 11									
1-9-1951	Jack Taylor	24	77	130	78	77	69	69	
No. 12									
1-12-1951	Debby Gabowitz	15	84	119	124	102	63	65	
No. 13									
1-30-1951	Kenneth Plemons	16	91	105	75	71	98	76	
No. 14									
2-8-1951	John Leno	46	118	144	142	80	65	66	3-Hr. test was taken at Mt. Sinai Hosp.—was wearing support for two years, but *not* during test.
No. 15									
2-15-1951	Andrew Skarinus	31	95	108	89	82	64	—	3-Hr. test at Mt. Sinai Hosp.
No. 16									
2-20-1951	Joseph Ring	46	79	121	122	95	87	74	
No. 17									This patient had a 4-Hr. gl. t. t.
6-7-1944	Joe Ryan	46	90	81	87	95	89	84	taken in 1944 with similar
2-21-1951									results.
No. 18									
2-28-1951	Mr. Sunshine	60	111	131	135	120	85	64	Had abdominal support for 2 yrs. but did not wear it during gl. t. t. Was sitting and resting.
No. 19									
3-13-1951	John Haffner	60	98	148	118	111	66	59	
3-20-1951			100	138	130	97	72	58	With support.
No. 20									
2-22-1951	Loretta Schuenler	25	77	111	90	66	65	62	
No. 21									
3-27-1951	Esther Rich	55	99	159	113	100	87	72	

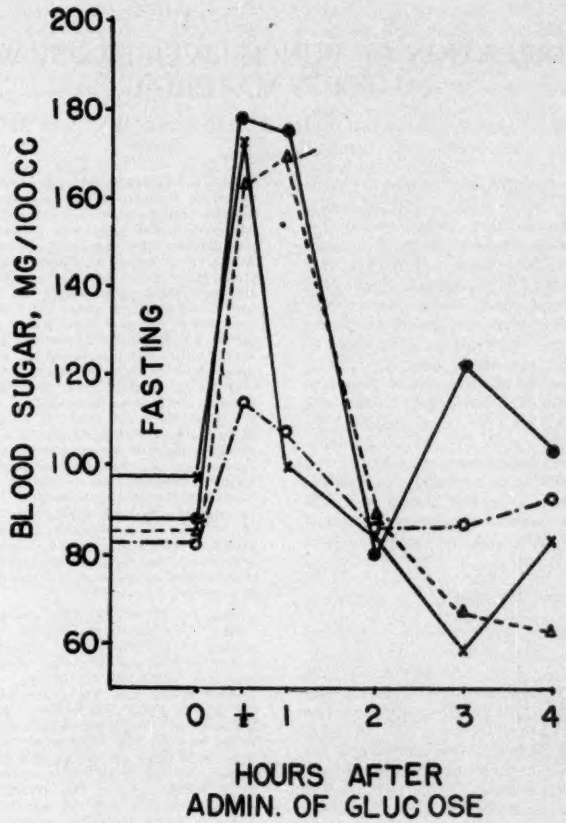

Figure 3

covered,—unfortunately, the profession at large so seldom recognizes the true nature of the case that finally, in addition to the morbid entity, the patient may be said to suffer also from a complication of doctors."

SUMMARY AND CONCLUSIONS

1. It is probable that many cases of functional hyperinsulinism and hypoglycemia are principally caused by visceroptosis.

2. The mechanism by which visceroptosis may effect functional hyperinsulinism is based on the twisting of the pancreatico-duodenal vein producing venous stasis in the pancreas.

3. Twenty-one cases along with 4-hour oral glucose tolerance tests (in five of the cases) are presented here in support of 1. and 2.

4. In these cases the use of pelvic supports provided marked and immediate relief and the symptoms of hypoglycemia were lessened.

5. The case histories reveal that 11 of the 21 were under 30 and one was 30 years of age. This suggests that the disease may be an important (and hitherto unrecognized) factor in the sudden deaths of young people following strenuous activity; (e.g., in swimming, and in flying. As the visceroptosis is not uncommon, and flyers are not examined for this condition, it is probable that many accidents in the air are due to hyperinsulinism caused by visceroptosis; as under exertion, the blood sugar may fall very rapidly as in Case No. 5).

6. The cases herein cited represent the last 21 cases of visceroptosis, who submitted to the 4-hour glucose tolerance test, to come under the author's care. The fact that all of them had disturbances of blood-sugar regulation implies that the condition described here is fairly common.

CORRELATION OF PUNCH LIVER BIOPSY WITH AUTOPSY MATERIAL

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NUMEROUS articles recently have proven the value of punch liver biopsy in the study of hepatic disease (1-21). Frequent references have been made to the correlation of needle biopsy specimens with autopsy material. However, there have been few studies of a long series of cases making this correlation. Schiff et al (20) presented a report of punch biopsy studies done on patients shortly before death or immediately after death and compared these observations with those of the necropsy findings. Because of the paucity of literature, we felt it worthwhile to review our series of approximately 700 needle biopsies and obtain the autopsy specimens of liver in every case possible. We hoped to determine and/or clarify the following points: 1) Whether the tissue obtained by punch biopsy can be interpreted as reliably and accurately as autopsy material; 2) whether diffuse hepatic disease was uniformly represented in needle specimens; 3) how frequently one can obtain a positive biopsy in focal disease.

SUBJECT MATERIAL

Approximately 700 liver biopsies were performed over a four-year period. The procedure used was described by one of us (M. C. F. L.) elsewhere (9). The Vim-Silverman needle via the subcostal approach was utilized in every instance. Out of this total 48 cases were selected for correlation studies. All 48 were autopsy cases and liver biopsies were performed for the most part within two or three months prior to the post-mortem. Correlations between needle biopsies and surgical biopsies were considered unreliable, inasmuch as the latter type of biopsy may easily miss focal lesions below the surface of the organ. To facilitate more critical analysis the cases were divided into the following groups:

1. Over-all correlation.
2. Focal and diffuse lesions.
3. Jaundiced and non-jaundiced cases.
4. Obstructive disease and hepato-cellular disease.

Over-All Correlation: Of the 48 cases studied, 45 correlated perfectly. Three cases were felt to be doubtful, and because of their peculiarity, are presented as follows:

Case No. 46: (See chart)—Patient was a 55-year-old white fireman, who entered the hospital on 5-5-50, complaining of abdominal distention, progressive anorexia, and edema. He was treated by his own physician and had had a paracentesis two weeks before admission. Past history was essentially negative and there had been no history of excessive alcoholic intake and he had always eaten well. Physical examination revealed moderate pallor, scattered spider nevi, minimal scleral icterus, and a hard, non-tender, smooth liver extending two fingerbreadths below the right costal margin. This organ was ballotable because of the marked ascites. His course in the hospital was progressively downhill and marked by recurrent bouts of hematemesis and melena. He expired on 7-6-50, two months after admission. Laboratory studies revealed abnormal liver functions. X-ray studies of the chest and the gastro-intestinal tract were negative. A punch liver biopsy was performed early during the hospitalization period and was interpreted as portal cirrhosis. His hospital treatment consisted of the usual management for this condition. Autopsy performed the day of his death revealed the primary lesion to be a primary carcinoma of the liver (hepatoma), with death from bleeding esophageal varices secondary to portal obstruction. In addition to the carcinomatous lesion there was present a diffuse portal cirrhosis. This case illustrates a type of lesion which can easily be missed with the biopsy needle, in spite of procuring an adequate section of liver tissue. Although hepatomas are relatively rare, the rather high frequency for coexistence with portal cirrhosis is apt to make the liver biopsy completely misleading, as was the situation in this case. A repeat biopsy or biopsies might well have established the correct ante-mortem diagnosis and should have been done in this case. It is especially indicated in cases of portal cirrhosis in elderly people with a large mass-like involvement of one lobe of the liver and in cases where the portal cirrhosis management seems to be refractory and the patient's course is progressively downhill.

Case No. 47: M. H.—This patient was an 81-year-old white female, admitted to the hospital on 6-16-47. She presented a history of abdominal pain, obstipation and weight loss over a three to four months' period. Examination revealed a patient who was confused, dehydrated, and presented evidence of marked weight loss. There was generalized lymphadenopathy, the glands being marble-sized, hard, and non-tender. Both hepatomegaly, and splenomegaly were elicited. Patient's course in the hospital was progressively downhill and patient expired three days after admission, on 6-19-47. Liver biopsy was performed prior to death and was interpreted as cholangitis with fatty metamorphosis. The reviewing pathologist seeing the same section felt that the periportal infiltration was of such a degree as to justify a diagnosis of lymphomatous disease, more specifically, that of lymphoblastoma. Autopsy interpretation was that of lymphosarcoma. It is our impression that knowing the clinical findings of diffuse lymphadenopathy, splenomegaly and hepatomegaly, the original pathologist studying the liver biopsy would have more seriously considered the diagnosis of a lymphomatous disease. This case is an excellent example of proper correlation between clinical and pathological material and an instance in which the examining pathologist must certainly be well oriented with punch biopsy sections.

Case No. 40: W. F.—Patient was a 35-year-old white male, admitted to the hospital on May 20, 1949 with complaints of severe epigastric pain of 36 hours' duration. In addition, he had had low back pain with sciatic radiation and a weight loss of approximately 35 lbs. in a 6-month period. Physical examination revealed an acutely ill patient, who was apparently having a moderate amount of pain, with marked dehydration. The liver was greatly enlarged, smooth and tender. Course in the hospital was progressively downhill, with fever ranging between 100° and 101°. Patient expired on May 31, 1949. Liver biopsy performed on 5-25-49 was interpreted as metastatic carcinoma to the liver. Autopsy diagnosis was that of malignant melanoma of the liver. Although a specific diagnosis of malignant melanoma was not made by means of needle biopsy, the interpretation of metastatic carcinoma was sufficient to outline the prognosis, course and management for this patient. The biopsy obviated further detailed diagnostic procedures and obviated the need of exploratory surgery. Although the three cases just presented did not correlate perfectly with the autopsy material, the findings of needle biopsy were such that one could not consider them entirely

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misleading in any instance. The gravest error was concerned with the interpretation of a possible curable and benign process, when very advanced malignant disease was the true situation, as in the second case presented. In the first and third cases the needle biopsy findings as interpreted did not alter the course, prognosis, or management given in each case.

CHART I

Case	*Biopsy*	*Autopsy*
1	Metastatic adenocarcinoma	Metastatic adenocarcinoma
2	Portal cirrhosis	Portal cirrhosis
3	Portal fibrosis* with stasis	Biliary cirrhosis
4	Metastatic adenocarcinoma	Metastatic adenocarcinoma
5	Metastatic adenocarcinoma	Metastatic adenocarcinoma
6	Metastatic carcinoma	Metastatic adenocarcinoma
7	Portal cirrhosis	Portal cirrhosis
8	Portal fibrosis; moderate hemisiderosis Portal fibrosis: severe hemisiderosis	Hemosiderosis with cirrhosis
9	Portal fibrosis	Portal cirrhosis
10	Portal fibrosis	Portal cirrhosis
11	Portal fibrosis	Portal cirrhosis
12	Portal fibrosis with bile stasis	Biliary cirrhosis
13	Cholangietic and fatty metamorphosis	Lymphocytic lymphosarcoma
14	Metastatic adenocarcinoma	Metastatic adenocarcinoma
15	Metastatic adenocarcinoma	Hepatoma (cholangioma) with cirrhosis
16	Metastatic carcinoma	Metastatic carcinoma
17	Metastatic carcinoma	Metastatic adenocarcinoma
18	Portal fibrosis	Portal cirrhosis
19	Metastatic adenocarcinoma	Metastatic adenocarcinoma
20	Metastatic adenocarcinoma	Metastatic adenocarcinoma
21	Metastatic carcinoma	Metastatic carcinoma
22	Portal fibrosis Portal fibrosis	Portal cirrhosis
23	Metastatic carcinoma	Metastatic carcinoma
24	Portal fibrosis	Portal cirrhosis
25	Metastatic carcinoma	Metastatic carcinoma
26	Portal fibrosis	Portal cirrhosis
27	Portal fibrosis Portal cirrhosis	Portal cirrhosis
28	Central congestion	Congestion with central degeneration and necrosis
29	Metastatic carcinoma	Metastatic carcinoma
30	Portal fibrosis	Portal cirrhosis
31	Metastatic adenocarcinoma	Metastatic adenocarcinoma
32	Fatty metamorphosis	Central degeneration and congestion
33	Portal fibrosis with bile stasis	Biliary cirrhosis
34	Metastatic carcinoma with biliary stasis	Metastatic carcinoma with biliary obstruction
35	Metastatic carcinoma	Metastatic carcinoma
36	Hemochromatosis with cirrhosis	Hemochromatosis with cirrhosis
37	Metastatic carcinoma	Hepatoma (cholangioma)
38	Probable hepatoma, possibly nodular degeneration	Hepatoma (liver cell type)
39	Metastatic melanoma	Metastatic melanoma
40	Metastatic carcinoma	Metastatic melanoma
41	Portal fibrosis with bile stasis	Biliary cirrhosis
42	Amyloidosis	Amyloidosis, Tuberculosis
43	Metastatic adenocarcinoma	Metastatic adenocarcinoma
44	Metastatic carcinoma	Metastatic adenocarcinoma
45	Portal fibrosis with bile stasis	Portal cirrhosis
46	Portal fibrosis with bile stasis	Hepatoma (cholangioma)
47	Infiltrating malignant cells, type undertermined	Lymphosarcoma
48	Hepatoma	Hepatoma (liver cell type)

*Indicates fibrosis of portal areas which could not be specifically classified.

Focal and Diffuse Lesions: Of the 48 cases there were 26 with focal lesions, of which 23 correlated perfectly. This impressed us as being an unusually high percentage for focal disease. We believe that our percentage is possibly higher because of two factors: 1) Repetitious biopsies; 2) Attempting to perform a punch biopsy in a focal lesion. Of the 48 cases there were 22 with diffuse disease in which the biopsy correlated with the autopsy material in every instance. An example of an unusual type of focal disease in which the correct diagnosis was made by punch biopsy is as follows:

Case No. 48: S. B.—This patient was a 60-year-old white male, who came to the hospital on May 25, 1950. He presented a history of progressive abdominal distention with mild intermittent abdominal pain and increasing weakness of one month's duration. Physical examination revealed a moderately jaundiced patient with a huge, non-tender liver, palpable down to the iliac crest with a suggestion of nodularity in some areas. Some ascitic fluid was detected in the flanks. Hospital course was that of progressive weakness and weight loss and patient expired 20 days after admission. Liver biopsy performed on June 1st was interpreted as that of hepatoma. Autopsy confirmed the needle biopsy impression. Here again the positive needle biopsy diagnosis obviated extensive laboratory and x-ray investigation and also obviated a surgical exploration. The hundred percent positive diagnosis of diffuse liver disease is understandable. It is extremely gratifying to make diagnosis of such conditions as amyloidosis, hemachromatosis, and others, when all other laboratory and diagnostic procedures have proved futile in making such a diagnosis.

Jaundiced and Non-Jaundiced Patients: Of the 48 cases, 20 were jaundiced, of which 18 correlated. Two cases did not and in both instances the lesion encountered at autopsy was that of primary hepatoma. There is unanimity of opinion that the punch liver biopsy is indeed an aid in the differential diagnosis of the jaundiced patient. The biopsy of the liver of patients with jaundice is not completely without hazard. There have been case reports in which external biliary fistula and biliary peritonitis have resulted following the punch biopsy. We have not encountered this complication.

Obstructive vs. Hepato-Cellular Jaundice: Of 20 cases of jaundice, 13 presented a clinical picture of obstructive disease and correlated on biopsy and autopsy. The remaining 7 were clinically intra-hepatic and correlated as such on biopsy and confirmed finally at autopsy.

Case No. 12: J. W.—A 64-year-old white male entered the hospital complaining of jaundice and singultus. His illness began one month previously with right upper quadrant pain of sudden onset, which was followed one week later with jaundice, weakness, anorexia, nausea, white-colored stools, and a weight loss of 20 lbs. Past history revealed a similar episode of jaundice with abdominal pain 11 years ago. He admitted excessive alcoholism for many years. Physical examination revealed a well developed, poorly nourished, deeply icteric, white male with a greatly enlarged, smooth and non tender liver. His hospital course was progressively downhill and he expired 13 days after admission. The laboratory work-up revealed a red cell count of 2,680,000 with slight uniform macrocytosis. The NPN was 75 mgm%. The urine was positive for bile and urobilinogen in 1:20 dilution. All liver function tests performed revealed moderate impairment of function. Liver biopsy was interpreted as obstructive jaundice associated with biliary cirrhosis. The patient's rapid downhill course precluded any surgical intervention. The autopsy revealed obstructive jaundice due to common duct stone with biliary cirrhosis of the liver.

DISCUSSION

That liver biopsy by the needle method is a valuable addition to the already well established clinical and chemical methods in diagnosis and for evalution of therapy is beyond question. However, in reviewing the literature relative to needle biopsy, one is struck by

the constant admonition of all groups that the value of the procedure is directly proportionate to the perspicacity of the individual providing the histological interpretation. It is imperative, therefore, that one be familiar with what constitutes abnormality due to disease and artefact due to the method. Such distinction can sometimes be extremely difficult.

We are in complete agreement with Keller and Sonetana in finding the needle biopsy more reliable than surgical biopsy of surface areas of the liver. In the latter it is extremely difficult at times to interpret inflammatory changes which have probably resulted from anesthesia, the trauma of surgery, or the primary condition necessitating exploration. This is not to be construed to mean, however, that the needle biopsy method is without artefactual change. This alteration is more or less constant and with experience can be properly identified and evaluated. In general the hepatic cell cytoplasm is homogeneous rather than granular; the nuclei are hyperchromatic and variably pyknotic rather than vesicular, as is usually the case in autopsy material. In sections prepared by the routine hematoxylin and eosin technique, the fibrillar character of the portal connective tissue is lost, as is the usually distinct junction of lobule and triad. Differential and specific connective tissue change resulting from compression may produce more serious difficulty in regard to the nature of any cells present in the portal areas. Such infiltrating cells are frequently hyperchromatic and pyknotic, rendering exact identification impossible or indefinite. This is undoubtedly the reason underlying the lack of correlation in at least one case (malignant lymphoma). The possibility of overcoming this compression distortion by allowing the sliver of tissue to "recover" in saline or similar medium before fixation is being investigated.

Morphologic Correlation: The anatomic correlation between the histologic findings in the needle biopsy specimen and the alteration present in the liver at autopsy has been excellent. These data, together with the mounting mass of evidence from many groups, leave no room for doubt regarding the diagnostic value of liver biopsy.

In all cases the biopsies were read and interpreted without benefit of clinical history to more rigidly evaluate the strictly anatomic change. Several instances are charted in which clinical information led to more accurate interpretation. In this study, for example, the biopsy in Case No. 13 was diagnosed as "cholangitis"; while the patient was in the hospital the pathological tissue report read "compatible with the clinical diagnosis of lymphosarcoma".

Of the total of 48 cases included in this study, the great majority represented either cirrhosis or metastatic carcinoma. Thus, in 19 cases (39.5%) the autopsy diagnosis regarding the liver was cirrhosis, either portal or biliary. Both types have been included for the purpose of correlation, since one is frequently unable on needle biopsy to completely separate the two. Of these 19 cases, a diagnosis of cirrhosis was made at biopsy in 18 (94.7%). In each instance also, the degree of fibrous tissue change was graded. A system of three grades was used and a difference of one grade was occasionally seen between biopsy and autopsy. This was not unexpected, however, in view of the time interval between the two procedures. In two (2) cases the fibrous change was associated with hemachromatosis and in each instance this fact was correctly interpreted in the biopsy specimen.

The second large group of similar cases in the series was metastatic tumor. Twenty (20) cases, (41.6% of total) were so classified at autopsy. Biopsy in this group was surprisingly accurate, the presence of tumor being noted in all cases. It is also interesting to note that each of the cases represents a single biopsy. Prediction of the primary site of the tumor on the basis of histologic morphology was always a challenge. However, in the average case one had to be content in suggesting two or three possibilities. The occasional metastatic malignant melanoma or small (oat) cell carcinoma was the exception.

Five cases presenting considerable difficulty in biopsy diagnosis were classified at autopsy as hepatomas (primary carcinoma of the liver). In one case this was suggested as a diagnosis on biopsy but the possibility that it represented active hepatic regeneration could not be excluded. At autopsy the tumor was extremely well differentiated. In two cases the tumor was of the bile duct type and in each biopsy was thought to represent a metastatic well-differentiated adenocarcinoma. Biopsy in one case did not include tumor. In the fifth case the diagnosis was clear-cut in both biopsy and autopsy material.

The single instance of amyloidosis presented no difficulty in diagnosis at biopsy.

CONCLUSION

A correlation study of 48 cases of punch liver biopsy material with autopsy specimens is presented. We are impressed by the remarkable correlation in both focal and diffuse disease. Punch biopsy material can be interpreted as reliably and accurately as autopsy material, especially by pathologists who have been oriented in the study of such tissue specimens, and particularly if the clinical history and findings are utilized to assist the interpreting pathologist.

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BULK AND ANTHRACENE IN THE TREATMENT OF FUNCTIONAL CONSTIPATION

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SODIUM CARBOXYMETHYCELLULOSE, one of many cellulose compounds developed in the past five years for the treatment of atonic constipation, was found to be well suited as a bulk producing medication (1, 2). Because of its freedom from side reactions and additional useful features, it was applied in a series of cases with uniform good results (3, 4). When ingested it produced no allergens, did not interfere with digestion or with normal bacterial activity. Its bulking action was found to be in the left half of the colon. It retained a greater quantity of fluid than most of the other bulk laxatives, integrated well with the fecal stream and passed with it as a formed stool.

Further investigation with this and other bulk forming materials led to understanding the reason for one failure that was common to all. Their action depended solely on their ability to expand and produce peristalsis. Continued use must therefore involve increasing dosage and greater distention to an already atonic bowel musculature.

Sufficient fluid intake at meal time and that consumed with medication is most important in the use of these types of laxatives (4). The role of fluid taken at other times plays a part in hydration but does little to assist in bowel activity. Since this fluid quantity cannot be assured to achieve the desired results when bulk laxatives are used, the question arose as to the use of additives to stimulate the neuromusculature of the bowel to prevent over-distention. Also, could the need for continued medication and dosage requirement be reduced?

Brewer's yeast and cascara sagrada, medications long used in stimulating bowel activity, were added to sodium carboxymethylcellulose and their effects noted on colonic motility. Accumulative action of the anthracine other than a temporary psuedo melanosis is not evident. Willow charcoal in five grain tablet form was used as an indictator to determine the rate of intestinal movement.

To find the average time required from ingestion to defecation, eighteen people without digestive complaints and in normal physical activity were instructed to take ten grains of charcoal with their evening meal and asked to note the passage of blackened stool. The mean period of this series was thirty-two hours. This may be termed normal intestinal behavior.

When three grams of the cellulose compound were added to the diet of the same group, the quantity of the stool was increased in one to eight ratio of the bulk consumed, but the motility rate was not greatly altered. Increasing the bulk dosage to six grams increased the mobility to thirty hours.

Fourteen people with normal digestive rates were given twenty grains of dried Brewer's yeast and three grams of the bulk with their evening meal. Of these three complained of abdominal distention one to three hours after taking the medication. Two stated that nausea persisted for several hours along with mild abdominal distress. These people also had diarrhea after six and ten hours with a highly irritating stool. It was felt that this response was upon an allergic basis because proctoscopic examination on the following day showed a thickened and reddened mucous membrane as far as the examining instrument could be passed as well as an increased eosinophilia. The average time of the other eleven cases was twenty-one hours.

Another series consisted of thirty-two people who were unrestricted in diet and activity. They were given six Natulose* tablets containing 7.5 grains of carboxymethylcellulose and 30 mg. of cascara sagrada extract and instructed to take these along with charcoal indicator daily. The reported average time was thirty hours. There were no digestive complaints; the stool was well formed and moist.

These findings indicate that the cellulose laxative agent could be markedly reduced to approach normal bowel tempo by the addition of safe medication. Where previously three to six grams of the bulk were required to activate the bowel, its combination with cascara gave results without overdistention with half the quantity of the bulk. The side effects noted with Brewer's yeast, that is gastric distress, distention and hypermobility of the digestive tract characteristic of allergic response, does not warrant its addition to this bulking material.

Treatment of functional constipation must be de-

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signed to accomplish two things. One is to re-educate the patient to understand his own bowel function. Food and fluid intake, habit adjustments, all must be thoroughly explained and understood. Secondly, the role of medication to assist bowel physiology must be clarified. He should be assured that no disease is present and that cooperation is necessary to solve his vexing problem.

In the aged, sedentary people and others who become chronic cathartic takers who rely on varied means to force bowel movements, a careful history should be made, and in the re-education period the fact that this condition is amenable to the prescribed treatment must be continually stressed. Dietary correction should be explained. An increase in vegetables and fruits and other foods rich in sugar should be added to the diet. Fats and dairy products, particularly milk which is constipating to many, may well be eliminated.

Natulose added to the diet is useful as a bulk and a mild bowel tonic. This can be used to help the patient over the period of readjustment. There can be a gradual withdrawal of the medication until bowel activity is achieved without drugs.

In post operative and rectal cases it becomes extremely important to regulate the fecal stream to the wounded anal outlet. The continued use of mineral oil leads to delayed healing, secondary infection and stricturing. It has been my practice to use mineral oil as an emulsion or anhydrous sodium phosphate postoperatively only during the hospital stay. A voluntary bowel movement usually occurs on the third postoperative day after which the patient may be dismissed. On leaving the hospital he is given Natulose tablets with directions to take two to four nightly with a tablespoonful of the mineral oil emulsion and a glass of water on retiring. After the tenth postoperative day the emulsion is stopped and the tablets continued until healing is complete. Within a two week period the patient should have no difficulty in passing a solid bolus of stool. By this time he has learned the importance of fluid intake at meal time and may continue his convalescence without further medication. The patient is seen twice each week at the office until symptom-free. Whenever patients continue to complain of dry stool following surgery or during medical care for constipation, it is found to be due to their lack of understanding or to the fact that some organic factor has been overlooked.

In over three hundred cases following anorectal surgery the mixture of carboxymethylcellulose and cascara sagrada in Natulose was used as bulk. Two to four tablets nightly were found sufficient to produce the required type of stool that dilated and cleansed the anus as it passed. There were no cases of impactions and rarely were aperients required.

CONCLUSION.

Constipation of atonic or functional type is not a disease. A dry stool indicates a dehydrated individual. Each patient is a problem unto himself, and education is of prime importance to obtain cooperation. Carboxymethylcellulose and cascara in dosage prescribed assists in the period of adjustment. Early reduced dosage and withdrawal is possible.

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CASES IN GERIATRICS AND THE PROBLEM OF THE PHYSICIAN'S OUTLOOK

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IT IS THE WRITER'S intention to concern himself with some considerations regarding a hobbyless physician who has reached the biblical age, and a review of some of his stock of geriatric experience since 1937.

The second part will prime the discussion. Since the greatest part of the writer's practice has been of a referral pattern, it has been intriguing to note the attitude of attending physicians of sixty years and over toward patients of same age: an attitude that suggests that organized publicity is the only way to remedy it. In current literature editorial attention has turned toward it, however sparingly. In 1938 the writer was informed that the extensive indexes of the Surgeon General's library in Washington listed no journal specializing in geriatrics, (1) which warranted the assumption that there was none, as against fifty-five specializing in diseases of childhood. The late doctor Nascher, in prefacing the first edition of his book (1916), pointed out that no American work on senile diseases had appeared in thirty years. "The causes of this neglect," said Nascher, "must be sought in the general mental attitude toward the aged. The spirit of veneration of ancestors and the aged, such as exists in China, does not exist among us." Dynamic activity in this field is, therefore, a necessity, evidenced, I believe, by the case studies that follow.

Case I: Male, age 72. His chief complaints were symptoms of indigestion, nondescriptive of a specific disease entity. On inquiry a malignant syndrome was conspicuously absent. He had been administered rhubarb and soda for many years, readily supplied by the pharmacist, and he had been hastily "gone over" physically by the family physician at frequent

intervals. The patient expressed resentment at being disposed of in an offhand manner by his doctor, remarking, "My old age is against me, he—the doctor—has no time nor patience for me." Simple gastric analysis yielded evidence of benign achylia gastrica. Hydrochloric acid therapy in adequate dosage and an attentive auditory apparatus were provided for him. The clinical response was gratifying.

Comment: The age of the patient was considered by his physician as being a contraindication to intubation, but he had overlooked the fact that alkalinization too is not without contraindications.

Case II: Female, age 68. Her digestive symptoms were: anorexia, gaseous distention, belching and pyrosis. She had not eaten meat since onset of her symptoms. She was usually constipated but at frequent intervals for many years, had had episodes of diarrhea. At the first examination she brought with her a large box with antacid powder she had kept refilled for several years. She was indignant that a much younger sister had been very thoroughly studied, while her symptoms were lightly thought of. She believed herself 'severely ill' and asked for a thorough survey. The physical findings were unremarkable. The blood chemistry was essentially negative and, a roentgenologic survey of the gastroenteric tract yielded no evidence of an organic lesion. Cholecystography showed a normal sequence. The stool under food control was negative for occult blood. The only positive laboratory finding was benign achlorhydria. Her digestive symptomatology and her diarrheal episodes—decompensating phenomenon in cases of achylia: gastrogenous diarrhea—responded to replacement therapy.

Comment: This case brings to mind what had probably been the stimulus to the work of the late I. L. Nascher, the notion that when an old person complained he was considered to be suffering from "old age" with no measure available to alleviate his troubles. This case as well as the first illustrate the many who are treated for clinical hyperacidity instead of being treated for anacidity with the indicated replacing therapy. It should be borne in mind that aside from exceptional cases, secretion of hydrochloric acid diminishes with advancing age. In absence of contraindications to intubation, gastric analysis is indeed a pathfinder to an unequivocal diagnosis. From a psychological standpoint, to the geriatric, a thorough diagnostic survey implies attention emanating from the juniors in his familial environment. The stream of new ideas and processes which pour forth from the cornucopia of medical science should be zealously applied alike to senescence and adolescence.

Case III: Male, 64, retired for years. He complained of epigastric distress, that food was tasteless, of a distaste for meat, diminished alertness and a general feeling of inferiority. He was well provided for by his children, but felt 'humble' and depressed. Physical findings were essentially negative. A general laboratory work-up was unremarkable except for marked hypochlorhydria (Free HCL 8 units, total acid 20 units) and low basal values (Minus 20 1st test, minus 24 2nd test). He was urgently advised to take some sort of employment in his sons' business. On inquiry this patient was found to be psychically rehabilitated. He has lost his stomach consciousness, and time moved rapidly for him on the job.

Comment: This case recalls an address on thyroid inhibition by Dr. C. H. Mayo (2): "All fires, whether those of our own bodies or otherwise, must have oxygen for combustion. If you are talking with people from forty to sixty years old, and you ask them something quickly and they look at you with their mouths open and ask 'what,' and they ask it the second time, 'what?' . . . give them a metabolic test . . . It is most interesting to see these people who have burned out their thyroids, without any pain or recognized trouble, but the chemical action is gone."

Analysis of six cases, grouped because of similarity in presentation of pattern, ages ranging between 68 and 84. Contraindications to intubation in some will become apparent from the histories. All of them harbored apprehension of the procedure and declined to attempt gastric analysis. Defective secretion in relation to age establishes that, model free acidity, normal or high, tapers off with advance in age to hypochlorhydria or total anacidity. On this basis HCL was administered with clinical response. Two of this group presented well defined contraindications to intubation: 1: A woman, age 85, had had a cholecystectomy followed by a stormy post-cholecystectomy syndrome. Shortly after, circulatory disturbance ensued. A cardiovascular study showed enlargement of the left ventricle, a systolic murmur over the aortic area due to atheromatous aortic changes, hypertension 190/115 accounting for the cardiac enlargement, general arteriosclerosis with myocardial damage as elicited from the electrocardiogram. Her digestive symptoms were clearly those of clinical hyperacidity and had been prescribed for cascara and rhubarb and soda; ingredients which do not inhibit repetition at the pharmacy. Two definite reasons for HCL therapy instead of antacid in this case were: 1, history of chronic gallbladder disease is commonly accompanied with anacidity, 2, her cardiovascular status called for a salt free diet. These essentials had not previously been considered. In 1940, this patient was placed on 30 minims of dilute HCL in various fruit juices, particularly fresh pineapple juice, with her meals. At this writing (March, 1951), she is faring along with the aid of vasodilatation and, anent her stomach symptoms, she stated that she feels very much alleviated and that she 'would not have a meal without the drops.'

Second Case: Male, age 58. Ten years ago he was diagnosed as having high blood pressure and had been treated for 'symptoms of dyspepsia.' Cardiological report reads, ". . . essential hypertension without cardiac or renal insufficiency." In March 1950, this patient suddenly lost vision in his right eye. Examination showed him able only to count fingers at three feet with his right eye, and revealed numerous hemorrhages in his macular region—hypertensive retinopathy. Blood pressure 190/110, enlargement of left ventricle. Electrocardiogram showed inversion of T wave in the first and second leads, the pattern being that of left ventricular strain. The keynote in the treatment is a salt-free diet. His clinical hyperacidity is now being combatted with small doses of dilute hydrochloric acid.

Comment: Four of these were apprehensive of the ill famed procedure of intubation. As described, the writer felt two were not fit for this procedure from a cardiovascular angle. By the Sahli Desmoid Reaction the physician may avoid the annoyance that certain patients show against intubation, and where contraindications arise.

The administration of alkalies has been practiced since an early period in the history of medicine and it still monopolizes the shelves in the pharmacies simply because gastric symptoms are readily interpreted in terms of clinical hyperacidity. In his early occupation as a pharmacist the writer recalls the gallons 'R&8' he dispensed, while the dilute hydrochloric acid on the shelf gradually ceased to be a colorless liquid. In the two cases of cardiovascular pathology calling for elimination of sodium ion from ingestion and the administration of hydrochloric acid, we furnish in addition to the appetizing influence of this drug, a strengthened line of defence against bacteriocidal action. As a synergistic fruit juice in which to take the dilute HCL, fresh pineapple juice is one of choice undoubtedly due to the proteolytic enzyme contained in the fresh fruit. It should always be borne in mind in dealing with the geriatrics that alkalinization has its contraindications, that these patients are apt to be hypertensives, nephritics, alkaloses, and some may have allergic phenomena conducive to alkalosis. HCL therapy is, therefore, the ideal replacing therapeutic agent. In the same vein of thought, in all cases of cholecystectomy of ages 50 or over, however mild the cholecystectomy syndrome, HCL could be used empirically without recourse to gastric intubation, on the basis that most cases of cholelithiasis usually have hypochlorhydria.

PEPTIC ULCER IN RELATION TO AGE

An elderly patient is not immune from duodenal ulcer. A female, age 72, pesented a picture of chronicity and intractability and described a classic post-pyloric ulcer syndrome. Gastric Chemistry yielded free HCL 88 units, total acidity 102 units. Roentgenology showed a marked duodenal deformity, without obstruction however. The warning by Lord Moynihan that "Persistent hyperchlorhydria is the medical term for the surgical condition of a duodenal ulcer," was not heeded by the family physician. His attitude

was wholly sentimental because of the patient's age. Instead of an advisably elective, an emergency operation had to be performed.

A companion case of advanced age: A male age 70 presented a symptom pattern of atypical cholecystitis, coupled with repeated nonvisualization of the gallbladder. The family physician dwelled upon the age of the patient, chose a minor diagnosis and insisted upon drug therapy. The writer argued that there is a difference between subacute noncalculous cholecystitis with roentgenologically visualized viscus, and chronic cholecystitis with stones but not visualized. He suggested that the absence of orthodox biliary colic attacks is compatible with silent stones. Jaundice set in. The family physician maintained that icterus would recede, that the patient was 'too old' for major surgery. However, jaundice deepened and the weight of evidence tipped the scales of medical opinion in favor of surgery. The operative findings were "Polypoid adenocarcinoma of the gallbladder with infiltration and cholelithiasis." Surgical intervention was rewarded with a post-operative survival of two years relatively asymptomatic until the terminal phase of his malignancy. This case needs no comment.

ANENT FORCED RETIREMENT

It may at first be strange to turn from the geriatric patient in search of an understanding doctor to a retiring physician in search of worthwhile occupation. In a sense, however, these are the two faces of a single coin, and one might even suggest that the solid linking them is the psychosomatic problem of age and retirement.

The writer recalls the policy of the N. Y. Medical Journal and Record that with each acceptance of an article submitted was a note asking what hobby the author followed. Invariably my personal answer was "the hobby of writing a paper." As age advanced it became apparent, that in the absence of extra medical activity, and when the 'legal age' of retirement becomes tinted with color of the yellow leaf, having no favorite pursuit is a regrettable loss. Truly the whole question of retirement, being chronological and not selective, is a difficult one and has evoked emotions not readily subdued. If one has years of teaching and activity in him, retirement to no extramedical activity of absorbing interest, constitutes a trauma on one's psyche. What fillip may one get in looking toward a calm and contemplative life? Dr. C. H. Mayo wrote in The Daily Northwestern of Northwestern University (57: No. 7, Sept. 30, 1936), "The teacher learns, too, that student days never end. Man is never too old to learn; further than that, he is never removed from the necessity of learning. He who loses the desire to learn may lose the desire to live." In these trenchant lines Mayo spoke the mind of a vast number of men. As long as the sun still shines on their backs, and they are neither laden with years nor by disorder of psyche or soma, the door need not be slammed because of 'legal age.' "A door to a new corridor out of which open other doors to other corridors in an endless perspective of opportunity," are the words of the great teacher, C. H. Mayo. In contrast to Mayo's philosophy, William Osler (6) advanced ". . . two fixed ideas. . . The first is the comparative uselessness of men above forty years of age," and the second ". . . the uselessness of men above sixty years of age, and the incalculable benefit it would be in commercial, political, and in professional life if, as a matter of course, men stopped work at this age." Such an attitude seems catabolic to the peripatetic philosophy of life—walking among the youths. For we need the gray heads to incite those ". . . between the ages of twenty-five and forty," depicted by our highly esteemed teacher as ". . . these fifteen golden years of plenty, the anabolic or constructive period . . ." It becomes apparent that the views of Osler are diametrically opposite to our modern concept of old age, that it can be molded into a form made graceful and acceptable to the old. Dr. Bernard Sachs, after sixty years of service, declared, "The joy of work is the joy of life. Don't let the Bibical three-score and ten affect you. To add to the years stop counting them." Thewlis (3) reflects on neglect of the aged, noting that most physicians treat them as they do the young, and, when the patient dies, attribute the death to 'old age,' not realizing that the organism demanded quite different drugs and handling. He rightly maintains that old age is neither a disease nor an effective cause of death. Willus (4) has graphically presented the phases of activity and declivity of life in an arbitrary biologic curve which if closely followed would mean the adoption of a "protective philosophy of life." For the individual who premeditatively follows the biologic curve and makes the necessary restrictive adjustments in life, middle age is the time you quit growing at each end, but continue in the middle, senescence would not imply declivity. Walt Whitman wrote,

"Youth full of grace, force, fascination!
Do you know that old age may come after you with equal
Grace, force, fascination!"

Obviously the poet rejected the concept that senescence is a disease. In a society based on material standards such as ours, even old age should not be shelved as useless, and we need but mention the brilliant achievements of such as Michelangelo in the arts, Jacobi, Keen and William Osler in medicine, Oliver Wendell Holmes in statecraft, Sigmund Freud in psychoanalysis, at very advanced ages. Hemmeter (5) wrote of Theodor Billroth, musical and surgical philosopher at sixty-five. "The soul of science breathed life into his teachings; the love of truth, with which Billroth was carefully saturated, made them real." To him belongs the honor of having performed the first successful extirpation of the larynx, as well as the first successful resection of the stomach. He had a store of energy and worked for months at a time from 16 to 18 hours a day—an example of pluck and determination. Lastly we may mention the many sided genius Schweitzer, and George Bernard Shaw, who started his career as a soap box orator and was still going strong shortly before he died.

The physician with no extramedical interest, should, all factors permitting, therefore be even encouraged to consider the practice of his art as his ultimate vocation. Andre Maurois pointedly remarked, "Growing old is no more than a bad habit which a busy man has no time to form." The keynote of mental hygiene for the geriatric individual is to die with his boots on. A lay scholar recently wrote me, ". . . The issue centers around the fact that, when retirement is selective, it is extremely embarrassing to say to Mr. Smith "you are old at 65, you must retire," while telling Mr. Jones, "you are still young at 65, keep on going." He concluded, however, "I have a strong suspicion that the Mr. Smiths, for whom retirement is desirable, are the

type who could have retired at 25 or 30, with profit to their community. Don't you agree?" Retirement should not be frozen mechanically with no fluidity and flexibility. Thewlis (5) rightly asserts, "The phase of life to which geriatrics applies does not begin at any special time; persons of thirty may present senile changes which should not occur till seventy or later." Dr. C. Charles Burlingame (6) the noted head of the Hartford Institute for Living, observed, shortly before his death, that some should retire at 40 and others at 75, and that it was "sociologically unsound and psychiatrically impossible" to retire all persons at 65. He wrote: "It is no longer considered good psychiatric practice, or good medical practice, for that matter to say 'you need a vacation,' which used to be the universal recipe when the medical adviser did not know what else to say. Sardonically enough, however, 'loafer's delight' or 'do nothing for a while,' with its etiological potentialities for mental and physical illness, is gradually receiving great impetus through pension schemes with enforced retirement. These erroneously assume that a man's goal is ultimate idleness. Too often, sudden decompression from carrying heavy responsibility is producing an emotional caisson disease which is gradually appearing in all doctor's offices in all specialties, even though not generally recognized. At least part of the cure is to have the *patient reassume* real responsibility."

In a word, the urge for retirement and pension schemes derives from the laziness of a few and the economic pressure of the many. Yet, as society seems to move toward levels of steady high employment, it surely should not be an excessive tax upon social imagination to produce an adequate degree of flexibility among the retiring group and adequate fluidity for the oncoming.

CONCLUSIONS

It must be recognized that there has in recent years been an improvement in both the social and the medical outlook on the problem of age. Let us confess, however, that these modest steps forward in public attitude and in medical learning and practice are as much owing to the demonstration of the nation's need for services of older men in World War II and since Korea as to a genuine reawakening on the part of either the public or the medical profession. In a sense, therefore, the place of the older group on both sides of the physician's desk has yet to be considered systematically and with foresight. With regard to the doctor's side, we lament the shortage of physicians as we are compelled to draft many for military service, but we do nothing to lower the obstacles to continued utilization of the skills of our older colleagues. With regard to the patient's side, we have not gone far or just enough in eradicating the 'old age' excuse for inadequate attention. We still have a shortage of geriatric literature that stands in bold contrast to the abundance of publication in pediatrics. To remedy this defect, given specialization, geriatrics should receive due recognition, on a par with other specialties, and the subject should be included in college curricula. Retirement as now in vogue is overmechanical and nonselective, with losses to professional life. Old age honors gold, paintings and tapestries. This should be our concept of senescence. Succinct and accurate is an aphorism of Nascher: Some are aged before they are old, some are old but are not aged. The 'old age' attitude on the part of general medicine should not go unchallenged. The range of interest in the geriatric patient should not be limited but should be permitted to widen and grow.

Thorough study of gerontology, on which preventive geriatrics is dependent, would help to bring the physiologic age up to par with the mental alertness of the individual, and public policy, in its broadest meaning of the organization of the activity of American society, must be reoriented to take into account the growing proportion of older people in our culture, together with their needs, and society's needs from them.

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PRESENT DIETARY CONSIDERATIONS IN LIVER DISEASE

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Nutrition behavior must be viewed in terms of the total behavior. While one may review the dietary implications in a disease, one should not forget that the whole nutrition picture is greater than its parts, or the sum of the parts. The liver is an important organ, but dietary essentials affect other parts of the body besides the liver even when one is thinking of present dietary considerations in liver disease, hence this review will fasten down those hinges that belong to the pathological physiology in addition to the important nutritive materials for life.

A critical evaluation of present diet therapy in liver disease makes a definition of terms important. Whether or not the pathogenesis of such liver diseases as cirrhosis of the liver involves lipids as a primary etiologic agent, a subject of considerable present day discussion, there can be no question somewhere in the pathogenesis lipids, cholesterol, lipotropic agents and fats must be discussed in relation to dietary deficiency diseases of the liver. The true nature of neutral fat, fatty acids, phospholids, cholesterol, Sf 10-21 particles cholesterol esters, lipotropic agents, and vehicles for

the removal of fat from the depots cannot be discussed in full at this point, the reader is referred to references (1, 2, 3, 4, 5, 6, 7, 8, 9, 10).

An ultimate understanding of the mechanism* of maintenance for good liver function is also involved in the picture of liver regeneration. Certain patterns are evident in our present day understanding of patterned reparative responses, particularly as protein is concerned with the supportive therapy. (11) (12) (13) (14) (15) (16) (17).

Food is an important factor in the environment which may contribute to the impairment of the liver. The integrity of the liver depends to a large extent on the food materials offered in the diet, elaborated as a result of the mix used in the G. I. tract, and utilized in response to the proportions found in the total pattern. A more penetrating understanding of the value judgements necessary in making the dietary order contribute to a maximum in the rehabilitation of the liver includes a dietary order of:

a. High protein of high biological efficiency offered in divided doses.

b. Protective calories offered chiefly from starches rather than sugars, the protein of plant origin, and lipoids of plant origin.

c. Vitamins, vitamers, vitagens and isotellic compounds which have been demonstrated as being interrelated with the calorie-carrying compounds.

d. Lipotropic factors in balance with the other aliments and nutrients.

e. Therapeutic concentrates and emphasis on those well chosen food supplements which convey the much needed restorative food agents in the right proportions.

f. Individually guided recommended daily dietary essentials that meet the need for total behavior in all areas, not just thinking of one "organ."

The association of dietary deficiencies with liver cirrhosis has long been reported. Being on a diet which is geared to enhance all dietary essentials, and particularly protein, vitamins, lipotropic agents, is an educational pursuit. Analysis of diets undertaken for the specific purpose of determining present day orders shows them to include: high calories, low cholesterol, low fat, high protein, high vitamin and mineral intake, possibly some restriction on sodium in some cases, protective in character, non-stimulating, laxative and adequate for the individual case.

All the data is not yet in for a complete review of the dietary factors in the etiology, but some of the literature references implicate too high a fat intake in the presence of too low a carbohydrate intake (below .6-.75 grams per kilogram) and too low a protein intake (below .5-.75 grams per kilogram in adults); deficiency of certain B-complex vitamins in the presence of high quotas of non-protective foods such as 1400 calories a day coming from refined sugars and milled grains in many of the so-called normal diets; use of beverages whch cannot be called upon to meet nutritional essentials.

Individual differences and individual variations in the amount and kind of materials offered is possibly the most discussed fraction of the present day liver damage literature. Variations in figures in the literature are such that some understanding of the factors responsible for the apparent discrepancies has become important to the intelligent interpretation of the standards quoted as acceptable for patterned reparative responses. A point in case is the vitamin A content of food. Most investigators recognize that all sources of carotene are potentially poor sources of vitamin A if the liver is not functioning to capacity. Hence vitamin A-1 and A-2 are much better choices than the 9 protein-carotenoids and cryptoxanthin at the onset of these liver diseases in which vitamin A pro-compounds are poorly handled. Moreover instead of 3000 I.U. of vitamin A, the standard is held up to 10,000 I.U. of vitamin A, or higher. In this 10,000 I.U. of vitamin A at least 6,000 I.U. will come from vitamin A-1 and A-2 instead of the provitamin-A groups. Vitamin A is a group and not a single entity.

For many years it has been suspected that a deficiency is never singular. Multiple dietary deficiency diseases may be handled by feeding the hungry tissues a diet replete in the right proportions of functional forms of the necessary dietary essentials. There are so many complementary, augmentary and supplementary interrelationships between one material and another that for purposes of illustration only, niacin is chosen to point up the complexity of the situation. A patient may use niacin to replace a part of the tryptophane in diets in which tryptophane is not present in high enough quotas, as for example on high corn diets which are low in lysine and tryptophane. However one may lower the amount of niacin needed by increasing the amount of riboflavin present. Riboflavin is important for the mobilization of vitamin A group and hence this fact makes B-complex vitamins important in liver function. Carotene conversion to vitamin A depends in part on an adequate supply of vitamin E group compounds. Vitamin A affects the metabolism of calcium, phosphorous and magnesium. Feeding an excess of vitamin A tends to prevent or to alleviate the toxicity of excessive doses of vitamin D. In avitaminosis A, B_1 requirement is increased. The amount and utilization of all nutritive materials is dependent upon the kind, assortment, proportions and balance of all other nutrients.

Attached are two levels of low fat, low cholesterol, high protein, balanced diets. It is not safe to drop below 2000 calories without vitamin-mineral supplementation.

*The mechanisms of maintenance of good liver function include:

a. Providing the richest dietary sources of the factors which have been missing in the diet, have been increased in need, have been excreted in excessive amounts, have been altered in metabolic function hence making them non-functional, have been diverted to some lesser function rather than the central objective, or are hence poorly utilized.

b. Shift the proportions to those that sponsor changes for the better in pathological physiology with the least expenditure of time, energy and materials.

c. Segregate the vehicles, acceptable from the long term point of view, from those foods and materials which may have short term interest but because of cost, inconvenience and unavailability are not suited to a diet that takes over for months and even years. Some plans for diets can be worked out in an institution that would not be practical at home.

CHOOSE A

DIET HIGH IN PROTECTIVE FOODS

Suggested Meal Pattern—low cholesterol, low fat
to Provide 3,000 Calories; 90 Grams Protein
60 grams of fat, high carbohydrate

Breakfast	Lunch or Supper	Dinner
Fruit—1 large portion	Fruit in season—1 serving	Protein food such as meat, fish, fowl game, egg dish, cheese dish, legumes or nut dishes. Not fried, no gravy.
Fruit juice—1 glass	Starchy vegetable such as potato, corn, brown rice	Starchy vegetables such as corn, sweet potato, Irish potato salad, peas, lima beans, etc. Seasoned with margarine.
Cereal with skim milk	Green or yellow vegetables 2/3 cup with seasoning-margarine	Salad or raw vegetable—3/4 cup
Toast—two slices, whole wheat	Bread—two slices, dark rye	Two slices bread and butter
Margarine—2 pats	Margarine—1 pat	Fruit for dessert—no pies, cakes
Milk—1 glass skimmed, hot or cold	Raw fresh greens or salad, French dressing—limited amount	Milk to drink—low fat Buttermilk Hot skim milk in soup or hot malted postum.
Egg or wheat germ or nut butter on bread, entire grain	Protein food, lean meat, fish, game, fowl, 3 oz., or souffle, fondue, cooked dried beans, peas, lentils, garbanzas, nuts (The choice should be varied)	
Brewer's yeast—15 tablets		
Drink plenty of fluids between meals, but avoid stimulating beverages.		
Eat at regular times.		

VALUABLE FOODS—SELECT FROM EACH GROUP ACCORDING TO TASTE, SEASONAL VARIETY AND COST

Individual differences in food selection should be recognized as far as possible.

Raw Vegetables (as tolerated)	Cooked Vegetables Seasonal choices	Fruits Highly pigmented	Protein Foods of High Biological value
Lettuce	Cabbage, green	Cantaloupe	Lean meat—all lean
Cabbage	Green asparagus	Pineapple	fish—not oily
Chard	Snap green beans	Grapefruit	fowl—without skin
Carrots	Green immature limas	Orange	game, only low cholesterol—make limited choice
Green Onions	Broccoli	Lemon juice	
Tomatoes	Brussels sprouts	Bananas	Yellow cheese
Fresh Greens	Swiss chard	Berries	Hard cheese should not be used alone, serve along with fruit and vegetable—Sk. Milk Jack
Romaine	Collards	Cherries	Cream cheese—limited
Watercress	Kale	Figs	Cottage cheese, dry curd
Celery	Mustard greens	Dates	Soybean cheese
Parsley	Okra	Currants	Soybeans—green or yellow
Radishes	Eggplant	Rhubarb	Dried beans—many types
Cucumber	Green peas	Melons	Lentils
Cauliflower	Spinach	Pears	Garbanzas
Turnips	Turnips	Peaches	Peas—green, frozen or dried
Rutabagas	Rutabagas	Nectarines	Seedmeals
Green peppers	Carrots	Plums	Brewer's yeast
	Greens of all kinds	Prunes	Wheat germ—defatted VioBin
CEREALS AND BREADS	Squashes	Fruit Cocktail	Bean sprouts, Alfalfa sprouts
Entire grain	Beets and tops	Fruit Nectar	Sunflower seed—limited
Unbleached	Mushrooms	Fruit Juices	Nuts—assorted—limited
Assorted kinds	Salsify	Raisins	Nut butter—limited amount
Supplemented.	Parsnips	Grapes	Peanut butter—limited amount
	Green soybeans	Persimmon	Egg whites used in dishes with defatted soybean flour, or cottonseed flour (Profio) or using various partially defatted nut flours as almond flour, peanut flour.
PLANT FATS IN LIMITED QUANTITIES		Avocado	
The word "butter" means plant fat or avocado or ripe olives or invisible fat in nuts, nut butter or oils.	Egg is limited to 1-2 a week.	Tangerine	Mushrooms, not sauted
		Apricot	Concentrates such as solubilized somogen or somogen granules or protinal powder or other low fat-high protein concentrates.
MILK PRODUCTS WITHOUT CREAM ARE SUGGESTED.		Applesauce	
		Baked Apple	
		Dried, fresh, frozen or seasonal fruits with the least possible sugar.	

LOW CHOLESTEROL DIET—2000 calories
LOW FAT-HIGH PROTEIN—HIGH VITAMIN—HIGH CARBOHYDRATE

FOOD GROUPS TO USE DAILY:

1 quart of skim milk or non-fat buttermilk or 3/4 cup non-fat-milk-solids, 3-4 ounces of lean meat or fish, or equivalent such as 1/2 cup hoop cheese, 2 ounces Skim milk Jack cheese, low fat; 1/2 cup cooked green soyas, 1/2 cup cooked beans, peas, lentils, garbanzas, soybeans or tofu. 1 cup black bean soup or green pea soup or legume and vegetable soup, 1 pint skim milk extra and large serving freshly cooked greens, 2 egg whites cooked with materials to make omelette without egg yolk, 3 ounces Life of Wheat, Vio Bin Wheat germ, Monticello, Ill. 1 1/2 ounces defatted almond meal used with egg whites in a main dish. 1 ounce nuts and serve at the same meal 1/2 cup green peas, English.

One large potato or sweet potato.

One serving starchy vegetable—peas, parsnips, legumes.

3/4 cup whole grain cooked cereal, assorted kinds or ready-to-eat types.

2 slices of whole grain bread, yeast type, at every meal

Tablefat—1 tablespoon, plant fat as margarine, nut butter or olives, avocado.

Vegetables—One raw food, fresh succulent, 1-2 cooked highly colored greens, 1-2 other vegetables, have a mixed, varied, and alternating diet. Protion 1/2-1 cup.

Fruit juices or fruit—1 raw fruit, 1-2 other fruits, dried, canned, frozen. Highly pigmented fruits.

Sweets are included if they include no egg or whole milk, 3 times a week. May use any simple dessert containing NO FAT. Fruit is the best dessert.

FOODS TO AVOID

(Only two eggs a week are allowed, on other days use alternates)

EGG AND EGG YOLK—fresh whole egg, dried, frozen, egg yolk in any form, some beverages containing egg powder, read the label on malted milk, eggnog, commercial breads

maybe glazed with egg, some meat loaf uses egg, egg-noodles, packaged mixes such as griddlecake, dumpling, waffles, doughnuts, cakes, muffins, pie crust, frostings made with egg, pudding bases, ices, some sherbets, ice cream, egg sauce as Hollandaise sauce, Tartar sauce, mayonnaise, commercial salad dressings, some candies, blanc mange, dishes prepared with eggs, baked, coddled, deviled, escalloped, fried, poached, scrambled, hard cooked, fried—French toast, pumpkin pie, banana cream pie, cocoanut cream pie, hard or soft boiled, egg yolk in sponge cake, gold cakes, Spanish cream, or sauces over meats.

ORGAN MEATS AND SHELL FISH—liver, tripe, sweetbreads, oysters, crab, brain, kidney, lung, thymus, liverwurst, giblets, sausages, frankfurters, wiener schnitzel, frog, pigeon, caviar, shad roe, snails, rabbit, shin of fowl, meal loaf or croquets containing animal fat, bacon, lard, grease.

ANIMAL FAT—bacon, chicken drippings, fat pork, ham, hog lard, butter, cream, whole milk cheeses are 44% animal fat, whipped cream, half-half, cream cheese, processed partially whole milk cheeses as in glasses, American cheese, Swiss cheese, Velveeta, Limburger, Pimiento.

MILK FAT—whole milk, some cultured buttermilks have cream added, yogurt, condensed milk, evaporated milk.

FRIED FOODS IN WHICH ANIMAL FATS ARE USED—fried ments on which there is suet. Doughnuts and fry cakes. All fats are to be limited to plant sources.

This diet furnishes 2000 calories, 85 grams of protein, 100-200 mg. cholesterol, less than 40 grams of plant fat, as limited in animal fat as possible, 1 g. calcium, 1.3 g. phosphorous, 15 mg. iron, Vitamin A 10,000 I.U. carotenoids, limited Vit. D, 1.5 mg. thiamin, 3 mg. riboflavin, 15 mg. niacin, 100 mg. ascorbic acid, and other vitamins and minerals. This diet should be supplemented by more fat-soluble vitamins.

MODIFIED BLAND—LOW FAT—ADEQUATE PROTEIN

Suggested Meal Pattern
to Provide 2,000 Calories; 85 Grams Protein
High in protective foods

Breakfast	Lunch or Supper	Dinner
½ cup fruit or fruit juice in season highly pigmented	Protein food such as pea soup, cottage cheese, skim milk Jack cheese, etc.—soybean curd, Tofu.	Protein food or dish as meat, fish, fowl, souffle, fondue, casserole, luncheon dish made with legumes—garbanzas. Lean selections, no gravy.
½ cup cereal with milk or slice toast with 1 tsp. margarine, use entire grain	Raw fresh vegetable salad—¾ cup with tsp. dressing.	Fresh succulent seasonal green salad type foods—¾ c. Serve with ½ lemon.
One glass milk, hot or cold, non-fat types.	Cooked vegetable—½ cup, green or yellow colored, fresh seasonal.	One starchy food—½ cup Potato, corn, parsnips, peas.
Egg, any way but not to be fried on two days a week, other days alternate	½ sandwich or slice bread with margarine—thin spread, or skim milk soups with potato.	Cooked, highly colored, seasonal vegetable—½ cup
Drink plenty of fluids between meals but avoid stimulating beverages.	Fruit for dessert—liberal amount. Limit all pies, cakes, cookies.	1 tsp. margarine or occasionally nut butter.
Brewer's yeast—15 tablets	Large glass of milk—12 oz. Buttermilk Reconstituted non-fat milk Hot skim milk used in soup	Large glass milk—12 oz., occasionally buttermilk or hot postum with malted milk, or skim milk.
Eat regular meals. Space the meals with 5-6 hours apart.	Mead Johnson's Vita Broth	Fruit in season with least possible sugar—¾ cup. No ice cream or rich puddings.

Sample Menu for One Day

Breakfast: Stewed prunes and apricot compote, oats with milk, hard cooked egg, skim milk. Brewer's yeast tablets 15 or 1 tablespoon dried brewer's yeast powder.
Lunch: Cottage cheese on Romaine, sliced fresh tomatoes, cooked carrots and celery, bread and butter, milk, peaches. Hot broth.
Dinner: Pot roast, peas, potato, cooked artichoke with lemon-sauce, milk, fruit cocktail.

VALUABLE FOOD GROUPS—CHOOSE ACCORDING TO YOUR TASTE, AND AIM FOR VARIETY

Fresh Vegetables and Salad Type Foods	Highly colored, freshly cooked vegetables	Seasonal Fruits	High Biological, low fat Protein Foods
Fresh grated carrots	Green asparagus	Ripe bananas	Lean Meat
Young green celery without strings	Green artichokes	Ripe persimmons	fish—not oily
Greens without stems	Green string beans	Ripe avocado	fowl—without skin
Romaine, watercress	Wax beans	Peaches	Hard cheese should be eaten with fruit and vegetable and not alone
Tomatoes	Lima beans, green	Pears	Skim milk Jack—or grating
Carrots, strips	Tender young peas	Apricots	Cottage cheese, uncreamed or Farmer's style, dry
Parsley	Squashes of all kinds	Cherries	Soybean cheese
(Lettuce is a gas-former)	Greens of all kinds	Nectarines	Garbanzas
Avoid foods in the onion and cabbage family.	Canned tomato, T. J.	Prunes	Lentils
	Carrots	Plums	Split peas—green or yellow
BREADS AND CEREALS	Okra	Fruit juices	Nuts—limited amounts
Entire grain	Eggplant	orange	Almond
Unbleached	Parsnips	grapefruit	Brazil nut
Supplemented	White potato	lemon	Cocoanut
	Sweet potato	prune	mixed nuts
TABLE FAT OF PLANT ORIGIN	Salsify	apricot nectar	Peanut butter—limited
	Pumpkin	apple juice	Soybean flour— defatted
DAIRY PRODUCTS LOW IN FAT	Beets	berry juice	Wheat germ—defatted
	Mushrooms	Fruit cocktail	Brewer's yeast, concentrates as Somogen.
LIMIT ALL NON-PROTECTIVE FOODS	Green soybeans	Seedless thin skinned grapes	
	Mature soybeans	Tangerines, Oranges, Grapefruit	
	Cooked celery		
	Zuccini		

Balance and proportion of certain B vitamins, cholesterol, certain sulfur containing amino acids, certain sources of labyle methyl groups, essential fat acids, fat, protein contributing food choices, and lesser understood recently discovered B_{12a} and B_{12b}, B_{14}, B_{15}, B_{16}, animal protein factors, intrinsic factors of Castle, etc. are covered to some extent by references (18-33). The biological Methylating agents can be synthesized at a rate insufficient to meet stepped up needs, hence the emphasis on increased exogenous sources of inositol, choline, betaine, methionine, B_{12a} and B_{12b}, associated with an increment in necessary amino acids, vitamins, minerals, carbohydrate.

SUMMARY

1. Choose high protein foods from plant sources. One quart of milk will supply 900 milligrams of methionine, the requirement must be met by increasing the non-fat milk supply and other foods. The protein requirement is by far the most important singular requirement, 10 grams of amino nitrogen daily, with protein at least 85-100 grams daily. Since fabrication of protein is based on liver function, not more than 14 grams per hour are offered. Too high a proportion of amino acids which do not lead to patterned, reparative responses will lead to poor protein utilization. Foods like gelatin are contraindicated. Foods with many presenting limiting amino acids that must have a high degree of augmentation, supplementation and complementation are to be limited in amount, such as corn zein, barley hordein. Every meal must contain 1/3 of the total protein and also total amino acids, with the planned feeding pattern arranged so as to make desirable functional units from the wide assortment provided in protective foods. Sulfur contributing amino acids plus B vitamins plus vitagens as choline and betaine must come from the protein carrying calories.

Counting the grams of protein is NOT enough, one must know the egg replacement value, net protein value, coefficient of digestibility, biological value, chemical net score, proximate composition and ease of supplementation, to evaluate a protein presenting limiting amino acids in the quantities used. Methionine is the most lipotropic amino acid. Tryptophane has some action.

2. Place in full review those agents which tend to eliminate hepatic fatty infiltration which arises from dietary deficiencies, the addition or subtraction of which is believed to influence the course of the disease. Not all lipotropic factors are of equal lipotropic action. Choline, choline precursors, inositol, betaine, B_{12a} and B_{12b}, folic acid and folacin, (Three portions methionine expressed in lipotropic activity are said to be the lipotropic activity of one part of choline) must be related to the lipotropic agent need. Labile methyl groups are supplied by betaine, choline and methionine. Choline and cystine can replace one-fifth of the methionine. Both fat and water soluble vitamins, or related materials must be evidenced. The brewer's yeast and non-fat milk solids offer a high percentage of the need for certain B complex vitamins. The lipotropic action of inositol is antagonized by the presence of certain fatty acids. Supply 1.8-3.0 mg. B_1. Offer 2.5-3.0 mg. or more riboflavin. Feed both tryptophane and 15-50 mgs. niacine. Pyridoxine, pyridoxal, pyridoxamine, B_6 is fed at 1.5-2.5 mg. levels. Folic acid and folacin must be offered with B_{12a} and B_{12b} and tyrosine and phenylalanine and vitamin C plus dehydroascorbic acid. The type of dietary fat is found to affect the intestinal synthesis of B-vitamins. All known B vitamins should be quantitatively estimated in the diets ordered. All sources of A, D, E and K groups may need to be provided in therapeutic proportions since fat is somewhat limited.

3. It is not enough to offer calories, the foods must provide a ready source of the vitagen glucose and the animal starch, glycogen. The type of carbohydrate that promotes intestinal synthesis of B vitamins and other factors which contribute to the needed materials for liver regeneration should be included in the daily dietary regime. Fruits of all kinds are preferable to sucrose, or sugar. Vegetables, potatoes, legumes and whole grains are better than refined, highly milled decorticated starches, grits, meals, flours, etc. Individual calorie need must be met up to 65% of the calories from carbohydrate foods and these should be vitamin-mineral-vehicles.

4. Instead of using 2 grams per kilogram, cut the fat to 1 gram per kilogram. Instead of using 40% of the diet as fat, cut the lipid intake to 15%-20%. Instead of taking 2000 milligrams of cholesterol, cut the amount to 100 to 200 mg. Instead of using animal fat use plant fat sources. Instead of eating fried food get most of the fat from invisible sources in the quantity needed.

CONCLUSION

1. Betaine, choline and methionine supply labile methyl groups (CH_3) for methylation. Choline and methionine favor other functions in addition to methylation which is a frequent mechanism by which the body may detoxify otherwise injurious substances. Sulfur contributing amino acids (methionine, methionine sulfoxide, glutathione, methionine sulfone, cystine, cysteine, cysteic acid, homocystine) and labile methyl groups must be present in the right proportions. By insuring a high protein intake of high biological efficiency, especially as chosen from plant sources, the need for amino nitrogen can be met.

2. A diet is described that provides:

a. 85-100 grams of protein, supplemented at each of three divided doses.

b. Lipotropic factors: Choline, inositol, methionine, sulfur containing amino acids, B_{12a} and B_{12b} active material, B. Vitamins.

c. Glycogen agents and carbohydrate in preponderance over fat, knowing that protein and carbohydrate protect the liver only if the protein is at high enough levels of intake. High carbohydrate diets do not protect the liver with only 5% calories as the protein from poor biological sources occupying the calories. Protective carbohydrates are used.

d. Vitamins, vitagens, vitamin like compounds with activity, isotellic compounds, and vitamers are in-

cluded in therapeutic amounts in (a) (diet*) (food) (exogenous food sources—concentrates) (b) bacterial synthesis by having the right flora (c) therapeutic orders—oral and other types.
Low protein diets* bring fewer vitamins of the B complex groups.
These and many more interrelationships between proteins, amino acids and vitamins, cannot be worked out without having a high enough quota of amino nitrogen, net protein, amino acids from assorted sources, chiefly plant.

e. Fat intake is lowered compared to the unusual past intake, and the plant sources take prominence over the animal sources, thus carrying less cholesterol.

f. Denatured foods which are leached of their many favorable enzyme systems are contraindicated. Not only foods high in fat, but those presenting many imbalances of amino acids and limitation in the necessary amino acids, and milled, decorticated impoverished sugars and starches are eliminated.

g. Planned feeding which meets individual needs are ever a matter of immediate concern to the trained medical personnel or homemaker, but only the food which the patient consumed in quantitatively estimated amounts should be charged with assisting in the patient's rehabilitation. To make the patient eat the food, his likes and dislikes must be considered and he should have his own food curriculum designed. Superimposed control will not lead to good educational practices, there must be the use of the democratic process in food selection, food preparation and services. He is an individual. He has ability and capacity for a certain type of meaningful dietary instruction, give him a voice in the dietary government.

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*A low protein diet is defined as one that furnishes .39 grams protein per kilogram for an adult or .75 grams protein per kilogram for children. The extrinsic factor is contained in high protein foods. Cystine requires the presence of choline. Tryptophane and niacin are interrelated. B_{12a}, B_{12b} and B_{12} active materials are enhanced by folic acid and folacin. Vitamin C, tyrosine and phenylalanine are interrelated. B_{12} and methionine show an interrelationship. Proline needs the presence of niacin. Tyrosine and phenylalanine need the presence of adenine. Glycine requires the preence of both adenine and nicotinamide. Para amino-benzoic acid is necessary in the metabolism of alanine, valine, leucine, aspartic acid, lysine, arginine, methionine and histidine.

ABSTRACTS ON NUTRITION

MOSS, J. M., AND MULHOLLAND, H. B.: *Diabetes and pregnancy, with special reference to the prediabetic state.* Ann. Int. Med., March 1951, 34, 3, 678-691.

A study of 450 pregnancies in 72 diabetics and prediabetics is reported. The fetal death rate in the diabetic group was 54.7 percent. During the years before the diagnosis of diabetes, a high incidence of large babies, toxemia, stillbirths, neonatal deaths and spontaneous abortions was noted. These complications began 30 years before clinical diabetes was manifest but they were most pronounced during the 5 years prior to the onset of the disease. The incidence of polyhydramnios and of spontaneous abortion is probably related to the control of diabetes, but the other complications mentioned are not. There were no fetal deaths in the cases of six pregnant diabetics who were given diethyl-stilbestrol, and such treatment should be routine in all diabetic women from the moment of conception. Latent diabetes should be looked for in all pregnant women by examining post-prandial urine samples. Those patients who have glycosuria, obesity or a family history of diabetes or who have previously had one of the complications of pregnancy common to diabetics, should have a three hour glucose tolerance test.

BASTENIE, P. A. AND KOWALEWSKI, K.: *Studies of the double and triple intravenous tolerance tests in normals, diabetics, in patients with liver disease and in those treated with cortisone.* Acta G. E. Belgica, 14, 4, April 1951, 201-222.

The studies indicated in the title showed that the repeated tolerance test detects the Staub phenomenon in normal subjects. It amplifies the abnormality of the hyperglycemic response obtained in liver disease, diabetes and under high dosage cortisone therapy.

VILTER, R. W. AND THOMPSON, C.: *Nutrition and the control of chronic disease: public health aspects.* Public Health Rep., 66, 20, May 18, 1951, 630-636.

Certain diseases which have hereditary features may be conditioned by the nutritional status of the susceptible individual. Again, a person may possess a metabolic defect requiring more than a "normal" intake of certain nutrients. The maintenance of adequate nutrition in the face of a chronic disease may do much to slow the progress of the disease. Obesity is related to hypertension, diabetes and arteriosclerosis, as well as to cholecystitis and gall stones. Excessive leanness due to caloric restriction predisposes to pulmonary tuberculosis and other chronic lung diseases. Mild deficiencies probably account for a great deal of chronic mental and physical ill health. Deficiencies of niacin, folic acid or vitamin B_{12} predispose to atrophy of the mucosa of the tongue and stomach and thus indirectly to leukoplakia and atrophic gastritis, both of which are precursors of neoplasms. The importance of nutrition to the aging of tissues is an urgent problem requiring much further research.

LEITNER, Z. A.: *The clinical significance of vitamin A deficiency.* Brit. Med. J., May 19, 1951.

The author reviews experimental and clinical knowledge of vitamin A, and stresses the importance of an adequate plasma vitamin-A level during the embryonal development and in some clinical conditions such as ocular, dermatological, hepatic and febrile diseases. He suggests supplementing the routine treatment of the acute stage of rheumatic fever with 40,000 to 50,000 I. U. of vitamin A daily. The same dose should be used in pregnancy complicated by infection or fever, especially during the first trimester.

VELIATH, G. D. AND SRINIVASACHAR, S.: *Cirrhosis of the liver in Madras Province, South India.* J. Indian Med. Assn., 20, 8, May 1951, 271-274.

121 cases of portal cirrhosis which came to autopsy were studied and the clinical histories compared with gross and microscopic findings in the livers. Almost half the cases showed a histologic pattern of fatty infiltration with varying degrees of fibrosis. These cases were classified as "deficiency cirrhosis", their cause being a deficiency in food of the lipotrophic factors such as B vitamin, choline and those proteins containing the essential amino-acid methionine. Nutritional deficiency is the most important etiological factor in the causation of hepatic cirrhosis in Madras Province, South India. Such cases are preventable and amenable to treatment if taken early. Sixty-four cases were classified as "post-necrotic cirrhosis", but the cause is unknown. Malaria, amebic dysentery and bacillary dysentery are not causes.

PEASE, J. C., SMALLPEICE, V. AND LENNON, G. G.: *Diabetes and pregnancy.* Brit. Med. J., June 9, 1951, 1296-1298.

A series of 25 consecutive diabetic pregnancies beyond the 28th week is presented. No mother died and 23 babies are living. Good results were obtained by adopting the following principles—(1) Working as a team with definite policy, (2) Careful diabetic control. (3) Induction of labor not later than the 36th week of pregnancy. (4) Careful neonatal control but without overtreatment of the baby. These results were obtained without the use of hormones. It is premature to make any dogmatic statement about the part that hormone therapy may play in the management of pregnancy in diabetic patients.

FORSYTH, C. C., KINNEAR, T. W. G. AND DUNLOP, D. M.: *Diet in diabetes.* Brit. Med. J., May 19, 1951, 1095-1101.

From the authors' experience of 50 diabetics given "free" diets and insulin over a period of 5 years, they are satisfied that if adolescents and obese patients are excluded, clinical control can be obtained. By "control" is meant freedom from hunger, thirst, pruritus, nocturia and ketosis, the maintenance of weight and energy and the avoidance of hypoglycemic symptoms. However, the degree of hyperglycemia and glycosuria and the daily fluctuations in blood-sugar levels are greater in such patients than in those on controlled diets. When very large doses of insulin are needed for clinical control, it is unjustifiable to keep patients on "free diets". However, in non-obese patients over 35 years of age, the "free" diet has worked out uniformly well. The authors subscribe to the theory that the incidence of degenerative signs is a factor in the disease's duration. The general import of the paper seems to be that there exists among older, non-obese pateints, suitable subjects for free-dieting.

FOY, H., KONDI, A. AND HARGRAVES, A.: *Response of megaloblastic anemia of pregnancy to crystalline penicillin G.* Brit. Med. J., May 18, 1951.

The strange case of a pregnant South African native whose megaloblastic anemia (associated with histamine-fast achylia) responded perfectly to injections of crystalline penicillin G is the second such case to be reported. The fact of this recovery gives birth to a number of speculations, the most provocative being the control of some systemic intoxication, such as might be produced by the bacterial flora of the intestine.

EDITORIAL

A NEW APPROACH IN THE ROENTGENOLOGICAL DETECTION OF EARLY GASTRIC CANCER BY "PHARMACO-RADIOGRAPHIE"

In spite of all the new methods of telecommunication, it sometimes takes a long time until scientific discoveries find their way across the Atlantic ocean.

By chance we were looking through the January, 1951, issue of the Archives des Maladies de L' appareil Digestif et des Maladies de la Nutrition, when roentgenograms, side by side with pathological specimens of early gastric cancer, caught our eye. It was an article by Guy Albot and Jacques Toulet, describing the early form of this dread disease. We stumbled over the word Pharmaco-radiographie, never having heard it before. We freely admit that our knowledge of the French language is very limited, and though we admire the work of our French colleagues, and have read their publications often (sorry to say not too often) we do not dare to discuss or abstract them as often as we would like due to our ignorance of the language.

But here, in this case, something new seemed to be presented. We got in touch with Guy Albot and received some of his former publications. And now we realized that some extremely important work has been going on of which we were entirely unaware, and, as far as we know, has been unreported in the American medical literature.

In order to improve the roentgenological visualization of the stomach, very often atropinization has been used. Guy Albot, in his studies, based on the work of other authors, especially R. A. Gutman, initiated a different approach namely: instead of relaxing the walls of the stomach, he applied drugs, firstly, for the purpose of increasing the pressure of the barium inside the stomach, thus better filling out all the crevices of the mucosa; and secondly, for the purpose of making the rigid parts more clearly visible through the violent contractions during the time of hyperkinesia. Three drugs are used for this purpose,—morphine, ipecac and insulin.

If an anomaly is found on films with full filling of the stomach, it is of importance to study the surrounding mucosa of the anomaly. The aforementioned chemicals apparently increase the turgor of the mucosal folds, let the folds become more pronounced, like somebody frowning. As the folds become more distinct, any abnormality, since it is rigid, and therefore cannot take part in the wrinkling of the mucosa will stand out clearly on the roentgenogram. Albot shows on his specimen the peri-cancerous change of the mucosa, which loses its distinct pattern, not only at the site of the cancer, but already at a short distance from the pathology. Of course, these areas have to be studied with the well known method of spot films and measured compression. That is nothing new. The new approach is that of using morphine, ipecac and insulin to stimulate the mucosal folds in order to study them better and discern all those, even very small parts of the gastric wall, which are rigid and the seat of a pathology.

We hope we have understood Albot's work, though we have failed to find all the answers to our own questions. We have been unable to find a reference to the amount and the way of application of the three drugs. We do not know how long after morphine was given that the roentgenological studies were performed. Also, side reactions to these tests are not mentioned, and, sorry to say, our own experience with ipecac in gastroenterology is nearly nil.

The illustrations of Albot's paper are very interesting and its new approach seems to be of the greatest importance, so that we have decided to bring this very unusual topic to the attention of our readers, though we realize that we have to wait for many answers to our questions before this new approach to the diagnosis of early cancer can be fully evaluated.

Albot's first publication appeared already in 1944. In a 1948 paper we read a good description of his method and a discussion of its basic facts, and its very important use in practical diagnosis. Only now are we able to bring this work to the attention of our readers and the larger circle of American gastro-enterologists. It took a long time, but we hope it will stimulate the scientists here and everywhere to new investigations.

Franz J. Lust, M. D.

BOOK REVIEWS

METHODS IN MEDICAL RESEARCH. Vol. 4, Maurice B. Visscher, Editor, 301 pages, The Year Book Publishers, Inc., Chicago, 1951, $7.00.

This is the fourth of a series of volumes devoted to the title subject, and deals with the following subjects,—Histochemical staining methods, Ed. George Gomori; Fluid and electrolyte distribution, Ed. Louis B. Flexner; Studies on gastrointestinal pressures, innervation and secretions, Ed. J. P. Quigley; and Tissue and culture methods, Ed. C. M. Pomerat. The gastrointestinal section includes the following subjects—Registration of digestive tract intraluminal pressures, Preparation of esophageal fistulas and gastric pouches. Methods for the study of external secretory function of the pancreas, Insulin-acidity test for determining integrity of vagal influence on the stomach, Methods of assaying gastric secretory inhibitors, and Methods for in vitro study of gastric secretion.

Each section is highly practical and the volume as a whole, like those previously published, is quite indispensable to the research worker. Friedman's chapter on esophageal fistulas and gastric pouches will prove especially helpful to those beginning the difficult surgery needed for successful dog-work. The practicing physician likewise will benefit by a careful study of each section.

FROM A DOCTOR'S HEART. Eugene F. Snyder, M. D., 251 pages, Philosophical Library, N. Y., 1951, $3.75.

A personal account of pain due to a coronary occlusion forms one of the main themes in this readable book. Additionally, the author, who fled Russia, desires better human relationships throughout the world today. Probably this book will prove most interesting to those who have lived through a personal episode of coronary thrombosis.

AMER. JOUR. DIG. DIS.

GENERAL ABSTRACTS OF CURRENT LITERATURE

PERRY, J. W.: *Some observations on the pathology of infectious hepatitis and allied conditions.* Med. J. Australia, April 23, 1949, Vol. 36, No. 17, 547-549.

The author believes that acute yellow atrophy of the liver may represent the extreme lesion in a liver which has been attacked by the specific virus of infectious hepatitis. When less severe liver damage occurs from this infection, the end result may be multiple nodular hyperplasia, a precursor of portal (or Laennec's) cirrhosis. All portal cirrhosis, however, is not a resultant of infectious hepatitis. Fatty infiltration of the liver derives from a wide range of causative agents, from phosphorus poisoning to amino-acid or vitamin deficiency. The author reports two fatal cases of Salmonella Derby enteritis in infants, one of whom developed a fatty liver, while the other one failed to do so, which proves that we must look to some other factor besides the infection to explain the fatty liver. He also described a fatal case of acute hepatic necrosis in a child, about 3 years old, probably due to the virus of infectious hepatitis.

BURTON-JONES, J. R. C. AND SHEPHERD, J. A.: *Rupture of the liver associated with parturition.* Brit. Med. J., May 28, 1949, 941-943.

A case is reported of rupture of the liver, with hemoperitoneum, occurring in association with parturition. Only one comparable case has been found in the literature. The immediate cause of the rupture was probably the muscular compression that occurs with the expulsive efforts of labor. A predisposing factor may have been the presence of liver damage brought about by pregnancy toxemia.

LITCHFIELD, H. R. AND MOSS, A. H.: *Obstruction of the bile ducts, hypoglycemia atelectasis.* Arch. Pediat., Mar. 1949, Vol. 66, No. 3, 97-109.

A six-pound, four ounce, new-born babe showed, immediately after birth, marked cyanosis with rales over both bases and 10 mgm. glucose per 100 cc. blood. Oxygen tent and continuous intravenous 10 percent glucose were used with 10,000 units penicillin every 3 hours for 3 days. The heart shadow was enlarged and x-ray showed bilateral congenital atelectasis. There were 150 erythroblasts per 100 white cells in the blood smear. On the eighth day jaundice was definite and remained during the hospital course. Gradual improvement occurred with lessening of the icterus index, better color in the stools which at first were clay colored, and the lungs showed increased expansion, and the blood sugar level rose. A diagnosis of congenital atresia of the bile ducts was made but operation postponed and finally never done, because the infant on bile salts by mouth greatly improved. The early hypoglycemia was thought to be due to a state of relative hyperinsulinism, the mother being non-diabetic. In this particular case there must have been bile duct obstruction which later resolved itself. Erythroblastosis is not unusual in association with atelectasis.

JURAJ KORBLER ET PAVAO FRANK: *Cancerous action of flax.* Arhiv. za Higijenu, Rada. Zagreb 1951, Vol. 2, Br. 1.

Series of experiments on animals in relation to researches of the cause of cancer of the lower lip in women who spin flax. By injection of finely ground flax-threads tumors appeared whose neoplastic nature can not be disputed.

Among 318 patients suffering from cancer of the lower lip, only four were women. (Lambe) Hueper found one woman to 10 men.

The well-known explanation why men are more susceptible to cancer of the lower lip than women is that there are more pipe-smokers among men than women. Already in 1739, J. Holland suspected this relation between pipe smoking and cancer of the lower lip. Samuel T. Soemering found in 1795, that it is not the smoke but the juices, forming in the pipe, which are the cause. R. Meltzer believes that this does not happen in the orient because there they smoke raw tobacco without preliminary preparation. But this is not quite true. Heurteux established, that in the Département Finistère in France men show cancer of the lower lip more frequently than women, though both smoke pipes with very short stems. Haberer found that in the Pusterthal in Austria, women are more often the victims and he explains this on account of women smoking pipes.

Köbler from the Radium Institute at Zagreb indicates that women who spin in the same way as peasants do, are particularly susceptible to cancer of the lower lip. The peasant holds the spool in one hand and the spindle in the other and passes the thread between her lips to moisten it with saliva.

In certain districts of Austria peasants use a similar method. Germanic peoples seem to think that such is the cause of cancer of the lower lip. Several observations lead to the conclusion that it is not only the traumatic mechanism which is responsible for the effect but also a certain specific influence from the thread itself. Several patients showed aggravation after having been exposed to flax-dust; example—part of the face particularly exposed to deposition of dust as the nasal furrows. This happened even when the patient never did any spinning.

The spinning material was always used in a raw state without preliminary preparation with mineral oils. These oils could not be responsible for the effects observed in Lancashire weavers. According to Henry, the Departmental Committee of the Home Office, of which Henry was then secretary, came to the conclusion that the cancer of these weavers could be attributed to the mineral oils.

Because all facts indicate the spinning material, especially flax, could exercise a cancerous action on the tissues, we have undertaken in the Institute of Hygene at Zagreb a series of experiments for elucidation of this relationship.

At the old Institute of Radium we had at our disposal some flax used by one of the women suffering from cancer of the lower lip. To ascertain that it really was flax, the material obtained from the sick woman was identified at the Botanical Institute of the University of Zagreb. The flax used by the sick patients came from *Linum usitatissimum*, a member of the flax family.

In every experiment we have chosen "epithelium" to observe the action of the flax. Experience teaches that in men the cancerous effect of flax, if it exists, must be looked for in an intimate and long contact of flax, with epithelium and not with any other kind of tissue. In our first series of experiments, white mice were injected under the skin in the mammalian region with a physiological solution of finely ground flax-threads.

In trying to control the biological processes which the animals underwent, we used the test described by H. L. Bolen and O. C. Gruner, recently recommended by N. Ph. Norman and A. M. Slicher and by M. Ivsic.

The first days after injection we had a large mortality. It was evident that death overtook especially those animals whose blood reaction was positive, which in our opinion shows the efficaciousness of the test. Animals with a positive reaction are frailer than others. Therefore it is better to eliminate them from the start.

The question still remains to elucidate which substance of the flax could be responsible for the apparition of the tumors. Flax is the most ancient plant used for spinning. *Linum alpinum* grows up to 2500 meters, *Linum maritimum* grows at the seashores. (Planchon) These plants were known even in the stone-age. The Bible speaks of garments made of flax. Egyptian tombs contained flax weavings and they knew the art of retting.

According to Richard flax seed used for brewing a tea or taken in a little water is a popular remedy against constipation.

Dust of the spinnings contains flax-wax, resembling ceresine, etc.; its ashes contain much SiO_2, Cl and CaO.

If at the start of the experiment the animal was healthy then the Bolen test was negative. This test became positive as soon as the tumor appeared.

ZELMAN, S.: *Liver and spleen visualization by a simple roentgen contrast method.* Ann. Int. Med., Feb. 1951, 34, 2, 466-478.

To avoid the dangers of thorotrast and other available agents, Zelman, in order to visualize the liver and spleen,

gives the patient a Seidlitz powder by mouth, and inflates the colon with air. Films are taken in the standing position at expiration, postero-anteriorly, 40 inch distance, with upright Bucky grid, one-half second exposure using 100 ma., and kilovoltage from 65 to 75 kv. The illustration reproduced in the article indicated excellent visualization of the liver and spleen.

CHINN, A. B., WECKESSER, E. C.: *Acute hemorrhage from peptic ulceration: an analysis of 322 cases.* Ann. Int. Med., Feb. 1951, 34, 2, 339-351.

In 322 cases of bleeding peptic ulcer, the overall mortality was 13.3 percent. Patients who continue to bleed after admission to hospital should be operated on in the first 24 to 48 hours. Those who stop bleeding should be operated on if bleeding begins again. Gastric resection is the operation of choice and the longer it is delayed, the less chance for success. Bleeding patients should receive a Sippy type of diet provided they are not vomiting and not in shock.

TOUSEY, W. H.: *Perforated peptic ulcers.* Northwest Med., 50, 2, 95-97, Feb. 1951.

The best surgical treatment is one which effects adequate repair in the quickest and simplest manner. Prompt healing occurs which in most cases is permanent. Performance of additional procedures is usually unnecessary and subjects the patient to unjustifiable risk. The old theory, "perforation cures the ulcer" is ridiculous, since the future of these patients depends on themselves and good medical management.

BOCKUS, H. L.: *The role of roentgenology in gastroenterology.* Am. J. Roentgen and Rad. Therapy, 65, 6, June 1951, 853-866.

In this Caldwell Lecture for 1950, Bockus reviews the important function of x-ray diagnosis in gastroenterology, brings up many thought-provoking points and emphasizes a number of details in which further light can only be shed by team-work between the expert gastroenterologist and the expert roentgenologist. Excessive gas noted anywhere in the G. I. tract is most likely to be due to swallowed air. Pyrosis, when it exists as an alternate symptom to pain in ulcer, demands further attention. Whether "pseudo-ulcer" is undetected ulcer or is due rather to motor dysfunction in the pyloroduodenal area, is another unsettled problem. The so-called "deficiency patterns" require further investigation to determine their true significance. Some roentgenologists are organicists and lack interest in the study of functional conditions such as "irritable colon". The relationship between specific deep-seated emotional trends and physiologic changes is becoming clearer. He deals also with a number of organic lesions of the digestive tract.

ISAACS, R.: *Diagnostic aids in the treatment of anemia.* Ill. Med. J., 99, 6, June 1951, 294-297.

Raphael Isaacs gives some very useful pointers for making a diagnosis of anemia from the stained blood smear alone. He suggests an index which is superior to the old "color index". It is obtained by taking the number of grams of hemoglobin, multiplying it by three and dividing by the first two figures in the red blood count. This tells us whether the anemia is orthochromic, hyperchromic or hypochromic. Hematocrit readings, unless accurately done, are misleading. He mentions a hemolytic anemia caused by faulty secretion of bile; interference with fat absorption leads to the decomposition of fats in the intestine with absorption of hemolytic fatty acids. This type of anemia disappears when extract of whole ox bile is given before each meal.

BUTLER, T. J. AND CAPPER, W. M.: *Experimental study of 79 cases showing the early post-gastrectomy syndrome.* Brit. Med. J., May 26, 1951, 1177-1181.

The authors used experimental distention of the jejunum with a balloon and also tried the effect of a mercury loaded bag in the gastric remnant. The sensation of central abdominal fullness is due to the distention of the jejunum. The other element in the syndrome,—the vasomotor component including sweating, tachycardia, palpitation—is due to the weight of food in the gastric remnant and can be completely duplicated by such inert substances as barium or a mercury bag. There is no difference in the blood sugar curve of those with or without the syndrome. Lying down abolishes the vasomotor symptoms but not the full feeling produced by distention of the jejunum.

WALTERS, W. AND BELDING, H. H.: *Clinical studies on 130 patients one to four years after vagotomy.* Proc. Staff Meet. Mayo Clin., 26, 11, May 23, 1951, 199-208.

The authors concluded that there is little place for vagotomy alone in the treatment of duodenal ulcer not only because of the relatively high incidence of recurrences of duodenal ulcer, but also because of the high incidence of persistent disturbances of motility. There is a place for vagotomy combined with gastro-enterostomy in highly nervous middle-aged males with large duodenal ulcers; in cases where the ulcer is small and pyloroplasty or gastroduodenostomy is used concomitantly; in some persons of high tension type with high free HCl, combined with gastric resection.

Vagotomy should not be done for gastric ulceration not only because of the high incidence of unsuspected malignancy but because of the high incidence of recurrence of ulceration, gastritis and motility disturbances. Vagotomy is valuable, however, in cases of recurring ulcer after adequate gastrectomy.

SCHIFF, L.: *The clinical value of needle biopsy of the liver.* Ann. Int. Med., 34, 4, April 1951, 948-967.

Needle biopsy of the liver has proved of great value at the Cincinnati General Hospital in the confirmation of clinical diagnosis as well as in alteration of the clinical diagnosis. When performed by physicians trained in the procedure and the patients kept in bed for at least 24 hours afterwards and transfused if necessary, needle biopsy of the liver entails very little risk. As a result of the biopsy, needless surgery may be averted or earlier operation invoked—advantages outweighing the risk entailed.

LEITNER, M. J. AND REESE, E. C.: *Endometriosis of the lower bowel.* Am. J. Proctology, 2, 1, Mar. 1951, 15-22.

The authors present a case to illustrate their theme and they also carefully cover the surgical problems involved in endometriosis of the bowel. Frozen-section examination at operation may be necessary to differentiate the lesion from cancer. Treatment should be as conservative as possible. Castration should be reserved as a last resort. Hormonal therapy (androgens) may be of value in controlling symptoms.

DEBUSSCHER, G.: *The circulation of the esophagus, stomach and duodenum: an anatomic and physiologic study.* Acta Gastro-Enterologica Belgica (Supplement May 1951) 271-314.

Although the circulation of the esophagus is rich, devascularization may occur, and in the dorsal portions this tends to necrosis, but neighboring organs may supply a collateral circulation. Gastric ulcer disturbs the gastric circulation only locally. Ligation of the vessel of a normal stomach may produce ulcers, yet the procedure cuts down acidity. The pyloric region is firmly vascularized but there is a lack of anastomoses.

MORRISON, L. M.: *The increased incidence of coronary thrombosis in chronic peptic ulcer.* Rev. Gastroent., 18, 5, 313-318.

There is a substantially increased incidence of coronary atherosclerosis, and of coronary thrombosis with myocardial infarction in chronic peptic ulcer. An evaluation of the prolonged use, over many years, of excessive dietary fat and cholesterol intake in chronic peptic ulcer patients, merits consideration as a potential cause of coronary disease and coronary thrombosis. Aldersberg, in discussing Morrison's paper, noted that both ulcer and coronary occlusion may have a common, thrombotic basis.

COLLINS, D. C.: *Enemata of gelfoam-milk suspension combined with thrombin-solution to control massive hemorrhage following anorectal surgery.* Amer. J. Proctology, 2, 2, June 1951, 60-63.

This is a preliminary report of the utilization of a suspension of Gelfoam (R) in milk followed by a thrombin solution and administered by an enema to promptly and efficiently control severe postoperative anorectal hemorrhage. Twelve patients

have been successfully treated by this method in the past months without the necessity of having to resort to secondary surgical procedures to stop the hemorrhage.

WAPSHAW, H.: *Significance of raised serum-enzyme levels in perforated peptic ulcer.* Brit. Med. J., May 5, 1951, 995-997.

Slight increases in the amylase and lipase levels in the blood occur in a small minority of peptic ulcer cases complicated by perforation. No histological cause for these changes has been found in the pancreas. A study of the clinical data in the present cases failed to yield evidence either for or against the view, supported by experimental work of others, that the increase in blood levels of the enzymes is due to their absorption into the circulation from the abdominal cavity.

MCNEALY, R. W. AND WOLFE, F. D.: *Polyps of the large bowel and their management.* Illinois Med. J., 99, 5, May 1951, 260-262.

More than 10 per cent of patients without any history of previous bowel disturbance will be found to have polyps in their large guts. When a polyp is of large size in a patient past middle life, it is safer to do a sleeve resection, since a local excision may offer almost as much difficulty and yet may leave tissue which is of doubtful malignant tendency. Adequate pre-operative preparation is essential.

SCHWARTZ, S. O. AND STEVENSON, F. L.: *Pernicous anemia associated with lymphosarcoma.* Illinois M. J., 99, 5, May 1951, 265-267.

The authors report a case of pernicious anemia associated with lymphosarcoma. Only five other cases of pernicious anemia associated with leukemia or lymphoma have been reported. Treatment of the pernicious anemia, which was successful, seems also to have reduced the peripheral lymphocytosis and leukocytosis without specific therapy directed to the lymphosarcoma.

VYNALEK, W. J. AND PALOUCEK, F. P.: *Torsion of the gall bladder.* Illinois M. J., May 1951, 268-269.

A diagnosis of acute appendicitis was made on a woman of 74, but on opening the abdomen, a large, free-hanging gallbladder containing 90 c.c. of dark fluid was found and removed. There was a half-twist in the gall bladder near its junction with the cystic duct. Pathologic examination of the specimen revealed an acute hemorrhagic infarction with almost complete necrosis of the gall bladder wall. She made an uneventful recovery.

SCHALM, L.: *Late and fatal complication after esophagogastrostomy.* Arch. Chirurg. Neerland, II, 2, 1950.

Schalm describes a fatal perforation of a peptic ulcer of the lower end of the esophagus into the pericardium, 18 months after anastomosis between the stomach and the dilated esophagus (due to achalasia of the cardia) according to the technique of Heyrovsky.

VAN AKEN, H.: *Stenosing peptic esophagitis.* Arch. Chirurg. Neerland, II, 2, 1950.

The author reports 3 cases of stenosing peptic esophagitis. A pathological study of resected portions of the diseased esophagi distinguished 3 stages in the pathological process. It can be differentiated from cancer. Treatment consists in resection of the diseased portion of the esophagus.

REVERS, F. E.: *Hyperparathyroidism,* Arch. Chir. Neerland, II, 3, 290-298.

Revers describes a case of hyperparathyroidism associated with diffuse calcification of the kidneys, who improved following a subtotal excision of all his parathyroid glands. He next enters into a review of the work of the Boston group on diffuse parathyroid hyperplasia and adenoma. Every case of renal calculi should be investigated for possible hyperparathyroidism. This involves estimation of the blood calcium, the blood protein level, blood phosphate, and alkaline phosphatase. The excretion of calcium in the urine is best estimated with Sulkowitch's reagent.

DONALD, H. R.: *Amebic dysentery.* New Zealand Med. J., XLIX, 274, 734-35, Dec. 1950.

In a letter to the Editor, Donald tends to play down the importance of finding E. histolytica in the stools in persons in New Zealand. He thinks that 10 to 20 percent of all persons in the world are carriers. Any condition or disease which lowers the resistance of the gastrointestinal tract such as bacillary dysentery or B-deficiency may cause an innocent commensal to become pathogenic and invade the gut. Infection by E. Histolytica already is endemic in New Zealand. The carrier rate is unlikely to be influenced materially by any practical system of examination, notification or treatment, neither is it likely to increase very much from poor hygiene. The pathogenicity of E. Histolytica in temperate climates is so low that this infection offers no threat to public health. The condition should not be made the scapegoat for invalidism.

GREENSTEIN, N. M., BARENBERG, L. H. AND STEINBERG, D.: *Relation of homologous serum hepatitis to prophylactic injection of human blood fractions.* Am. J. Dis. Child., 81, 2, 218-225, Feb. 1951.

A study was made of the incidence of homologous serum hepatitis in a series of 13,755 children between the ages of 3 months and 12 years who received intramuscular injections of human plasma, serum and gamma globulin for prophylaxis against ward contagion, and it was found that 35 children with jaundice were admitted to hospital, of whom 25 had not received previous injections, and 10 had been given such injections. In the 10 children who had received injections, jaundice developed more than one year after injection. In none did jaundice develop less than one year after injection, thus ruling out homologous serum jaundice whose incubation period never is greater than 150 days. This good record was due to using a restricted and selected pool of blood fractions derived from known patients.

AMERICAN BOARD OF INTERNAL MEDICINE SUBSPECIALTY GASTROENTEROLOGY

APPROVED RESIDENCIES AND FELLOWSHIPS IN GASTROENTEROLOGY AS OF SEPTEMBER 10, 1951

Michael Reese Hospital, Chicago, H. Necheles, M. D., Director, Dept. G. I. Research, Ass. Res. and Residencies offered, 1 Beginning of Service (1949) 1/1, 7/1, No stipend.

Lenox Hill Hospital, New York City, H. A. Rafsky, M. D., Attending Gastroenterologist, Ass. Res. and Residencies offered, 1, Beginning of Service (1949) 7/1, Beginning stipend (month) $50.00.

Hospital of the University of Pennsylvania, Thomas E. Machella, M. D., Chief of the G. I. Section, Ass. Res. and Residencies offered, 1, Beginning of Service (1949) 7/1, no stipend.

Temple University Hospital, Philadelphia, Pa., Harry Shay, M. D., Professor of Clinical Medicine, Head of Gastrointestinal Division. Ass. Res. and Residencies offered, 1, Beginning of Service (1950) 7/1, beginning stipend (month) $50.00.

Veterans Administration Hospital, Richmond, Va., John P. Williams, M. D., Chief of Service, Ass. Res. and Residencies offered, 1, Beginning of Service (1950) 7/1, 1-2 yrs., beginning stipend $3,000.-00 per annum.

Veterans Administration Hospital, Long Beach, California, F. W. S. Modern, Chief of Professional Services, Ass. Res. and Residencies offered, 1, Beginning of Service (1950) 7/1, 1 yr., beginning stipend $2400 to $3000 per annum.

Letterman General Hospital, San Francisco, Calif., James O. Gillespie, Col. MC, Chief of Medical Service, Ass. Res. and Residencies offered, 1, Beginning of service (1950) 1/1, 7/1, beginning stipend according to Army rank.

Graduate Hospital, University of Pennsylvania, Philadelphia, Penn. One year full time in Gastroenterology. Henry L. Bockus, M. D., Professor of Medicine.

AAAS PHILADELPHIA MEETING, DECEMBER 26-31, 1951

The 118th Meeting of the American Association for the Advancement of Science, the annual meeting for 1951, will include programs of all 18 of the Association's sections and about 45 participating societies. Focus of the approximately 225 sessions will be Convention Hall, adjacent to the University of Pennsylvania's School of Medicine and its associated hospitals; there will be some meetings in the downtown hotels, especially the Bellevue-Stratford (headquarters) and the Benjamin Franklin (zoologists). Programs of particular interest to those in medicine and experimental biology include:

SECTIONAL PROGRAMS

AAAS Section C-Chemistry: Eleven sessions, including one on Medical Chemistry, December 28; two on Forensic Sciences December 29; and two on Reaction Mechanisms, December 26, 27.

AAAS Section F-Zoological Sciences: A symposium, Estuarine Ecology, jointly sponsored by the American Society of Limnology and Oceanography, American Society of Zoologists, and the Ecological Society of America, December 30; a two-session symposium, Sex in Micro-organisms, jointly sponsored by AAAS Section G, the American Society of Protozoologists, American Society of Zoologists, and the Botanical Society of America, December 30.

AAAS Subsection Nm-Medicine: Four-session symposium on Abnormalities of Lipid Metabolism, with special reference to arteriosclerosis, December 29, 30; plus a medical scientists' dinner, December 29, at which Malcolm Soule will deliver a vice presidential address.

AAAS Subsection Nd-Dentistry: Three sessions, including a symposium on Fluoridation as a Public Health Measure, December 28, 29.

AAAS Subsection Np-Pharmacy: Six sessions, cosponsored by the American Association of Colleges of Pharmacy, American College of Apothecaries, American Society of Hospital Pharmacists, and the Scientific Section, American Pharmacists, and the Scientific Section, American Pharmaceutical Association, December 27-29.

AAAS Section O-Agriculture: Four-session symposium, Public Health Aspects of Soil Science, December 27-28.

PROBLEMS OF SOCIETIES

Oak Ridge Institute of Nuclear Studies: Two-session symposium on Radioisotopes in Medicine, luncheon, December 28; a series of lectures either December 27 or 29.

American Society of Protozoologists: Eight sessions of papers, a luncheon, and a business meeting, December 27-29.

American Society of Zoologists: Fourteen sessions of papers, December 28-29, also symposium, December 27; demonstrations, December 28; zoologists' dinner and Biologists' Smoker, evening of December 29; and symposia, December 30.

Herpetologists League: Conference session, December 28.

Society of Systematic Zoology: Five sessions including breakfast, business meeting, and symposium, The Classification of Animals, December 28: two paper-reading sessions, December 29.

American Microscopical Society: Three sessions, December 27-29, including a symposium on microscopy.

Biometric Society, Eastern North American Region: Six sessions of papers on biometry, December 27-29.

Society for Research in Child Development and AAAS Section N: Four sessions including a symposium, Biochemistry of Nutrition in Human Growth, December 27.

Alpha Epsilon Delta Premedical Honor Society: Luncheon and afternoon program, December 28.

American Industrial Hygiene Association: A special program in connection with inauguration of the new AAAS Section P-Industrial Science.

SPECIAL SESSIONS

AAAS Presidential Address by Roger Adams, December 28. Evening lectures of Sigma Xi, and RESA, December 26, 27. Evening lectures of Phi Beta Kappa, and Phi Kappa Phi, December 29, 30.

AAAS Annual Exposition of Science and Industry: The 1951 edition of the Association's Exposition again will total about 150 booths and will fill the arena of Philadelphia's Convention Hall. In addition to leading publishers, instrument makers, and suppliers of scientific materials, there will be technical exhibits by prominent manufacturers of pharmaceuticals and biologicals. On or near the exhibit area will be the Fifth Annual International Photography-in-Science Salon and the AAAS Science

Theatre which, almost continuously, will show the latest foreign and domestic scientific films.

Housing: Coupons for hotel reservations will appear in Science, beginning with the issue of August 24, and The Scientific Monthly, beginning September.

Registration: Main Registration at Convention Hall; Fees, $2.00 for members of the AAAS, spouses, and bona fide students; $3.00 for nonmembers. Advance registrants pay 25c more but receive the General Program in December, by first-class mail.

U. S. VITAMIN CORP. BUYS ARLINGTON CHEMICAL CO.

U. S. Vitamin Corporation, New York, N. Y., has announced, through its President, H. B. Burns, the purchase of time-honored Arlington Chemical Company of Yonkers, N. Y. The 72,000 square foot plant, together with a large new building to be constructed thereon, will be utilized to enlarge the services of both U. S. Vitamin and Arlington to the medical and pharmaceutical professions.

Steeped in tradition as a manufacturing pharmaceutical house, Arlington has pioneered in the introduction of many highly regarded ethical products since its inception in 1887, almost three quarters of a century ago. A protein preparation first marketed in 1893 was the forerunner of today's widely used protein hydrolysates, of which Arlington's Aminoids is one of the best known. Other notable Arlington preparations include Neo-Cultol, its line of allergens, Elixir Lactopeptine, and Hemaboloids.

U. S. VITAMIN EXPANSION

Mr. Burns states that the present and planned new manufacturing and laboratory facilities, together with an additional score of chemists and other scientists, will lead to the introduction of several new Arlington products.

New products will definitely be issued by U. S. Vitamin Corporation, makers of such outstanding items as Vi-Syneral, Vi-Syneral Vitamin Drops, Vi-Aqua, Methischol, Vi-Litron and Poly-B. Also scheduled for expansion is another subsidiary of U. S. Vitamin, Casimir Funk Laboratories, Inc., headed by Dr. Casimir Funk, who originated the word "vitamine."

Arlington personnel will be maintained and expanded under the direction of the U. S. Vitamin Corp. The 160 field representatives of U. S. Vitamin Corp. (and its affiliate Casimir Funk Labs., Inc.) will take over the promotional and sales activities of Arlington. Main offices of U. S. Vitamin will continue at 250 E. 43rd St., New York 17, N. Y.

CLINICAL RESEARCH AT ROBINS

Appointment of William R. Bond, M. D., as director of clinical research for the A. H. Robins Co., Inc., Richmond, Va., has been announced by E. C. Robins, company president.

Dr. Bond was graduated in medicine from the Medical College of Virginia in 1928, after having qualified as a graduate pharmacist seven years previously. He is a special lecturer in physiology at the Medical College of Virginia and, from 1929 to 1934, was professor of physiology and associate professor of pharmacology at the same institution.

In his new affiliation, Dr. Bond will be closely associated with Dr. Eugene L. Jackson, medical director of the Robins Company. Among the products of this oldest ethical drug company in the South, are such leading prescription specialties as Donnatal, Pabalate, Entozyme, Robitussin and Phenaphen.

Dr. Bond was engaged in medical research for the Schering Corp. from 1938 to 1946. More recently he has served as medical director for Charles Haskell & Co., Inc.

The new clinical research director is a fellow of the American Medical Association and a member of the Southern Medical Association, Medical Society of Virginia, Richmond Academy of Medicine, Association for the Study of Internal Secretion, Virginia Acadamy of Science, New York Academy of Science, American Association for Advancement of Science, American Pharmaceutical Association and the Virginia Section of the American Chemical Society. Dr. Bond completed his pre-medical course at the College of William and Mary. To his medical training at Richmond he added courses in biochemistry at Harvard Medical School. The doctor's hobbies include geography, astronomy and natural history, while on social occasions he demonstrates talents which have won him membership in the Society of American Magicians.

CIVIL SERVICE

The United States Civil Service Commission has announced a Medical Officer examination for filling the following positions in St. Elizabeths Hospital, Washington, D. C: Rotating Intern, $2,200 a year; Psychiatric Resident, $3,400 to $4,200 a year; Surgical Resident, $4,200 to $4,700 a year; and General Practice Resident, $3,400 to $3,800 a year.

To qualify for these positions, all applicants must have had appropriate education in an approved medical school. Applicants for psychiatric, surgical, and general practice resident must also have completed a 1-year internship. In addition, applicants for surgical resident appointments must have completed a 2-year residency in surgery. No written tests are required. The maximum age limit is 35 years.

Persons who applied for but did not receive appointments under the Commission's 1950 examination for the above positions should apply for this new examination.

Further information and application forms may be obtained from the U. S. Civil Service Commission, Washington 25, D. C., from Civil Service regional offices, or from most first and second class post offices. Applications will be accepted until further notice by the Committee of U. S. Civil Service Examiners, St. Elizabeths Hospital, Washington 25, D. C.

SOMETHING NEW

After 40 years behind the dispensing counter, S. A. Mortland of the Pioneer Drug Co., Yakima, Wash., has discovered a new use for a prescription tablet he never knew before.

"This morning a patient rushed in with her prescription number and asked if we would give her one of those Pabalate tablets," Mr. Mortland wrote to A. H. Robins Co., of Richmond, Va., recently. "She was downtown to buy paint and linoleum for her bathroom and wanted to be sure to get them in the same shade as the Pabalate tablets.

The High Protein, Low Fat Diet in Coronary Atherosclerosis

Recent advances in the dietary and medical management of atherosclerosis have improved the prognosis of this degenerative vascular disease. No longer is atherosclerosis regarded merely as a progressive disease of advancing age with an inevitably fatal termination, but rather as a metabolic abnormality subject to therapeutic management.

According to a recent four year study,* it is indicated that the course of atherosclerosis as it involves the coronary vessels may be favorably influenced by an adequate diet low in fat (20 to 25 Gm.), high in protein, and adjusted to the caloric needs of the individual for maintaining ideal weight. Lean meats, at both the noon and evening meals, can contribute importantly to the protein adequacy of the diet.

Reported effects of this diet included reduction in the mortality rate of patients with coronary thrombosis and myocardial infarction, reduction in total serum lipids, neutral fats, and chylomicron and lipomicron counts. An increase in well-being and capacity for work in the clinical subjects was also demonstrable. These effects, in part, were attributed to reduction in weight in the obese and "high normal" weight subjects, to psychotherapeutic results, to adequate vitamin A intake ensured by addition of a vitamin A concentrate to the diet, or to metabolic changes induced by a decreased fat intake.

Meat, a favorite protein-rich food, can contribute valuably to the protein needs of the atherosclerotic patient as well as to the normal individual. The protein of meat contains all the essential amino acids in proportions required for good growth and upkeep of tissues and for the maintenance of tissue functioning and general resistance to infection. Meat is also a rich source of iron and of vitamin B complex, including niacin, pyridoxine, riboflavin, thiamine, and the newly discovered vitamin B_{12}.

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*Morrison, L. M.: Arteriosclerosis: Recent Advances in the Dietary and Medicinal Treatment, J.A.M.A. *145*:1232 (Apr. 21) 1951.

The Seal of Acceptance denotes that the nutritional statements made in this advertisement are acceptable to the Council on Foods and Nutrition of the American Medical Association.

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Obedrin Tablets permit full utilization of the appetite depressing action of methamphetamine hydrochloride but eliminate the central nervous stimulation, so the patient does not suffer from nervous irritability and insomnia.

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Obedrin Tablets and the 60-10-70 basic diet will permit loss of weight with minimum discomfort, thus inviting patient cooperation.

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*Semoxydrine Hydrochloride	5 mg.
Pentobarbital Sodium	20 mg.
Ascorbic Acid	100 mg.
Thiamine Hydrochloride	0.5 mg.
Riboflavin	1 mg.
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*Methamphetamine Hydrochloride

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A COMPLIMENTARY PAD OF DIET SHEETS AND A TRIAL SUPPLY OF OBEDRIN SENT TO PHYSICIANS ON REQUEST.

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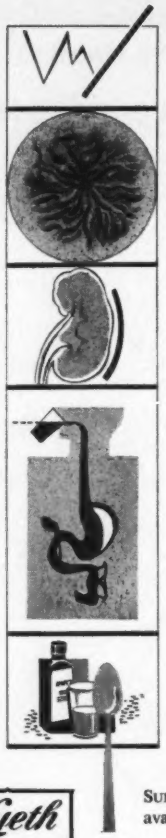

relieves pain promptly	stops gastric corrosion
promotes rapid healing	provides a soothing protective coating over the ulcer
no kidney damage	imposes no added burden on kidney function
never causes alkalosis	buffers gastric contents moderately; permits normal neutralization of alkaline secretions of upper intestine
no acid rebound	even in excessive doses. Does not cause unphysiologic alkalinity and consequent acid secretory response
pleasant to take	smooth, creamy, pleasing taste and texture

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SUPPLIED: Liquid, bottles of 12 fl. oz. Also available: Tablets of 5 grains and 10 grains

After 15 years of clinical use, the most widely prescribed medication for peptic ulcer—

AMPHOJEL®

ALUMINUM HYDROXIDE GEL • ALUMINA GEL WYETH

Wyeth Incorporated, Philadelphia 2, Pa.

in peptic ulcer–

NEW CONVENIENT CHLOROPHYLL THERAPY

Chloresium

MUCINOID
Tablets • Powder

for rapid relief of symptoms and tissue repair even in intractable cases

All the advantages of CHLORESIUM POWDER* are now available in convenient *tablet* form: same unique combination of healing agent plus antacids in a mucin-like base — same superior clinical results — and in a form that's easy to take.

highly concentrated, purified water-soluble chlorophyll promotes healing of affected areas, duplicating the outstanding results obtained in treatment of external lesions.

specially prepared, mucilaginous okra base clings tenaciously to mucosal walls, protecting against erosion and maintaining the chlorophyll in prolonged contact with the lesion.

prompt, sustained antacid action — without undesirable side effects — provided by magnesium trisilicate and aluminum hydroxide.

packaging: CHLORESIUM MUCINOID is available in bottles of 50 and 200 tablets and in boxes of 25 powders.*

*CHLORESIUM POWDER will continue to be available in boxes of 25 envelopes but will now be sold under the name CHLORESIUM MUCINOID.

RYSTAN COMPANY, INC. Mount Vernon, N. Y.

She had left her sample at home!"

The Pabalate tablet is a fine clear yellow. The Company replied to Mr. Mortland suggesting the Persian Rose color used in Pabalate-Sodium Free in case the lady wishes to redecorate her bedroom.

NEW PRODUCTS

The S. E. Massengill Company announces the addition of two new prescription preparations to its line of products.

The first of these is Capsules Semhyten indicated for the treatment of essential hypertension and as a prophylactic measure in combatting malignant hypertension. Semhyten makes possible, with a single medication, the basic control of the hypertensive patient. The product Semhyten is not cumulated and once the proper dosage level has been established, maintenance medication can be continued for long periods without fear of toxic reactions. Semhyten is available in bottles of 100, 500 and 1000 pink-topped capsules.

The second product is Perle Semvimin. This preparation supplies the most important of the trace elements and therapeutically significant amounts of vitamins, and is indicated as a diet supplement to promote optimum well-being of the patient. Semvimin is available in bottles of 100 and 1000 red perles.

Nutley, N. J.—A new, potent curare antagonist which acts within one-half to one minute—Tensilon Chloride 'Roche'—has just been announced by Hoffmann-La Roche Inc. Tensilon is useful whenever a curare antagonist is needed either to terminate the action of curare when no longer required or to counteract overdosage. It is particularly valuable in abdominal and pelvic surgery, in endoscopy, in shock therapy, in patients whose muscle spasm is treated with curare, and in other conditions in which curare is used. Tensilon is also a potent antagonist for d-tubocurarine, Flaxedil and dimethyl-tubocurarine (Metubine or Mecostrin). It is, however, ineffective against Syncurine and Mytolon. Administered by intravenous injection in 10-mg (1-cc) doses, Tensilon is available in 10-cc multiple-dose vials, 10 mg per cc. Chemically, Tensilon Chloride is (3-hydroxy-phenyl) dimethyl-ethyl ammonium chloride.

NEW ANTI-ANEMIA PREPARATION INTRODUCED BY WINTHROP-STEARNS

A new hematinic preparation called Fergon Plus, designed for therapy in most types of anemia encountered by physicians, has been introduced by Winthrop-Stearns Inc., as an addition to its Fergon line.

Fergon has been extensively prescribed for many years in the treatment of anemias due to iron deficiency, such as those in infancy, pregnancy, malnutrition and gastro-intestinal diseases. Fergon Plus, available in the form of soft gelatin capsules, is a special preparation of ferrous gluconate and vitamin B12, folic acid, gastric mucosa, ascorbic acid and liver fraction 2.

Besides iron deficiency anemias, therapeutic indications for the new product are anemias responding to oral vitamin B12 or folic acid therapy, including megaloblastic anemias of pregnancy and infancy and macrocytic anemia of tropical and non-tropical sprue. In pernicious anemia, although not a substitute for parenteral therapy with vitamin B12 or liver injection, it may be used in the cases which respond satisfactorily to the oral administration of Vitamin B12.

In addition to its therapeutic uses, Fergon Plus may be administered as a prophylactic, constituting a dietary supplement and maintenance source of folic acid, iron, vitamin B12 and ascorbic acid. It is supplied in bottles of 100. Therapeutic dose is 3 capsules taken 2 or 3 times daily, and, for prophylaxis, one capsule daily.

RICE, HOSKINS CITED FOR WARTIME SERVICE IN INTELLIGENCE MISSIONS

Dr. Justus B. Rice, medical research director of Winthrop-Stearns Inc., and E. L. Hoskins, president of Cook-Waite Laboratories, Inc., were recently presented with Certificates of Appreciation for service with the Technical Industrial Intelligence Committee, Joint Chiefs of Staff, during World War II.

In a ceremony at Governor's Island, N. Y., Lieut. Gen. Willis D. Crittenberger, commanding general of the First Army, made the presentation.

Before V-E day, Dr. Rice and Mr. Hoskins were selected from the pharmaceutical and dental manufacturing industries to obtain information on Germany's wartime medical and dental advances. They spent three months during the war on separate investigations, interviewing captured scientists and manufacturers in the respective fields.

Chief objective of the missions was to determine whether the data could be applied to the war against Japan. Although the Japanese surrendered shortly thereafter, the material gathered in these investigations has since proved useful to American industry.

Dr. Rice was selected particularly for his experience in the field of tropical diseases. His confidential report, now unclassified, revealed, among other new chemical processes, that the Germans had developed a blood substitute as a by-product of synthetic rubber manufacture. Considerable progress has since been achieved in the United States.

Mr. Hoskins' report revealed that generally, the practice of dentistry in Germany had deteriorated during the war because of the shortage of essential materials. Considerable information was found, however, concerning the manufacture of artificial teeth with an acrylic material instead of dental porcelain. This information contributed to American research and development of better materials.

For the mission, Dr. Rice and Mr. Hoskins served in uniform with the rank equivalent to that of colonel, in the G-2 or intelligence arm of SHAEF.

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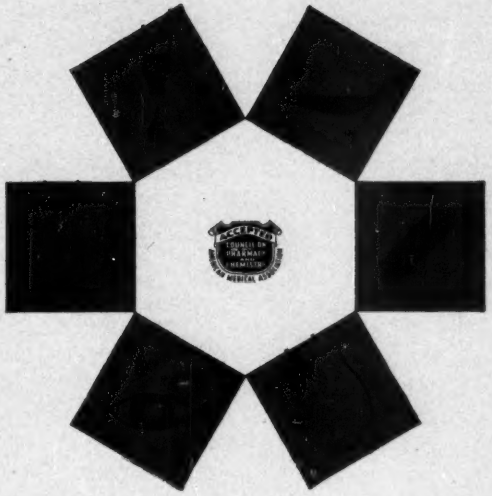
Terramycin



dosage forms for

optimal simplicity and flexibility

For oral administration, Terramycin is supplied in Capsules of 3 potencies, as well as in a palatable Elixir and concentrated Oral Drops made possible by the unique solubility of this great antibiotic agent. Terramycin is the only broad-spectrum antibiotic available in these 3 forms which simplify oral therapy for patients at all age and weight levels.

For the treatment of severe fulminating infections, Terramycin Intravenous permits the attainment of immediate high serum concentrations. And for topical therapy of ocular infections, Terramycin is available as an Ophthalmic Ointment and an Ophthalmic Solution, both well tolerated and effective against a wide range of micro-organisms causing infection of the eye.

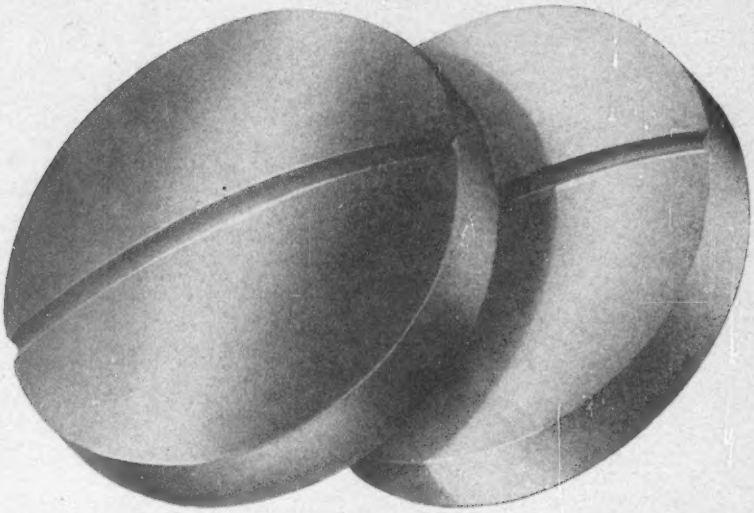
supplied: **Capsules:** 250 mg., bottles of 16 and 100; 100 mg., bottles of 25 and 100; 50 mg., bottles of 25 and 100; **Elixir:** 1.5 Gm. in 1 oz. diluent; **Oral Drops:** 2.0 Gm. in 10 cc. diluent with calibrated dropper; **Intravenous:** 10 cc. vial, 250 mg.; 20 cc. vial, 500 mg.; **Ophthalmic Ointment:** 5 mg. per Gm., ⅛ oz. tube; **Ophthalmic Solution:** 25 mg., 5 cc. dropper-vial.

Antibiotic Division **Pfizer** CHAS. PFIZER & CO., INC., *Brooklyn 6, N. Y.*

NOW

2 Banthine Dosage Forms:

THE TRUE ANTICHOLINERGIC IN PEPTIC ULCER IS NOW AVAILABLE AS:



Banthine *and* Banthine with Phenobarbital

"More and more importance is being attached to the role of hypermotility of the stomach in the causation of ulcer pain and less to the influence of simple hyperacidity.

"Banthine studies have demonstrated that while it does lower gastric acidity in most patients, its most important function is this same decrease in hypermotility with almost immediate relief of pain."*

DOSAGE FORMS:

Banthine (50 mg.), scored tablets.

Banthine (50 mg.) with Phenobarbital (15 mg.), scored tablets.

*Editorial: Promise in Peptic Ulcer, West. J. Surg. *58*:445 (Aug.) 1950.

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SEARLE *RESEARCH IN THE SERVICE OF MEDICINE*